

10/069,202

=> d his

(FILE 'HOME' ENTERED AT 14:49:50 ON 22 JUL 2004)

FILE 'REGISTRY' ENTERED AT 14:49:57 ON 22 JUL 2004

L1 STRUCTURE UPLOADED  
L2 50 S L1  
L3 1153 S L1 FUL  
L4 STRUCTURE UPLOADED  
L5 0 S L4 SAM SUB=L3  
L6 0 S L4 FUL SUB=L3  
L7 STRUCTURE UPLOADED  
L8 18 S L7 SAM SUB=L3  
L9 401 S L7 FUL SUB=L3  
L10 752 S L3 NOT L9  
L11 STRUCTURE UPLOADED  
L12 18 S L11 FUL SUB=L10  
L13 734 S L10 NOT L12

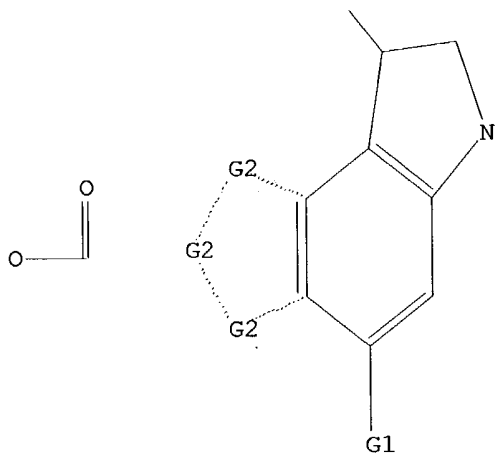
FILE 'CAPLUS' ENTERED AT 14:56:28 ON 22 JUL 2004

L14 112 S L13

=> d l1; d l4; d l7; d l11; d his; log y

L1 HAS NO ANSWERS

L1 STR



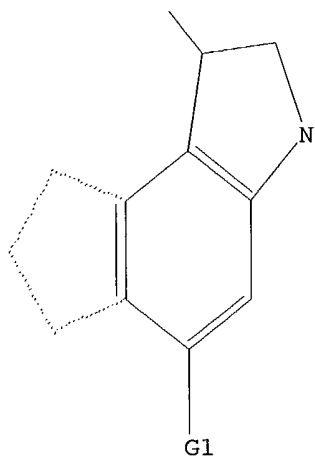
G1 O,S,N

G2 C,N

Structure attributes must be viewed using STN Express query preparation.

10/069,202

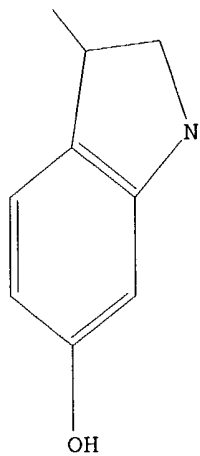
L4 HAS NO ANSWERS  
L4 STR



G1 O,S,N  
G2 C,N

Structure attributes must be viewed using STN Express query preparation.

L7 HAS NO ANSWERS  
L7 STR

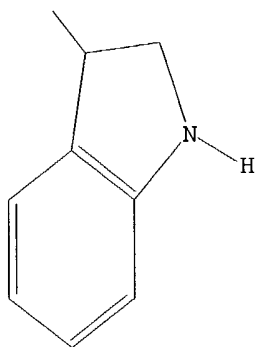


G1 O,S,N  
G2 C,N

10/069,202

Structure attributes must be viewed using STN Express query preparation.

L11 HAS NO ANSWERS  
L11 STR



G1 O,S,N  
G2 C,N

Structure attributes must be viewed using STN Express query preparation.

(FILE 'HOME' ENTERED AT 14:49:50 ON 22 JUL 2004)

FILE 'REGISTRY' ENTERED AT 14:49:57 ON 22 JUL 2004

L1 STRUCTURE UPLOADED  
L2 50 S L1  
L3 1153 S L1 FUL  
L4 STRUCTURE UPLOADED  
L5 0 S L4 SAM SUB=L3  
L6 0 S L4 FUL SUB=L3  
L7 STRUCTURE UPLOADED  
L8 18 S L7 SAM SUB=L3  
L9 401 S L7 FUL SUB=L3  
L10 752 S L3 NOT L9  
L11 STRUCTURE UPLOADED  
L12 18 S L11 FUL SUB=L10  
L13 734 S L10 NOT L12

FILE 'CAPLUS' ENTERED AT 14:56:28 ON 22 JUL 2004

L14 112 S L13

10/069,202

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	561.61	831.39
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-82.32	-82.32

STN INTERNATIONAL LOGOFF AT 14:59:03 ON 22 JUL 2004

10/069,202

L14 ANSWER 1 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2004:486392 CAPLUS  
DN 141:59683  
TI Exopolysaccharide micelles for delivery of active molecules  
IN Beaudet, Nicolas; Dupont, Claude; Lemieux, Pierre; Simard, Eric;  
Goyette, Philippe  
PA Technologies Biolactis Inc., Can.; INRS (Institut National de  
Recherche  
Scientifique)  
SO PCT Int. Appl., 31 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004050057	A2	20040617	WO 2003-CA1899	20031204
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

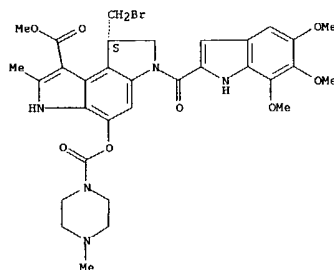
PRAI US 2002-430690P P 20021204  
AB The present invention relates to a delivery system for delivery of a pharmaceutical active mol. to a patient, the delivery system comprising a population of exopolysaccharide (EPS) micelles, each micelle defining a core for containing the active mol. The active mols. are selected from the group of DNA, RNA, protein, peptide, peptidomimetics, virus, bacteria, neutraceutical products and pharmaceutical agents. It is found that EPS has synergistic effects with some anticancer drugs and can also upregulate expressions of some genes. For example, i.m. injections containing paclitaxel

L14 ANSWER 1 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
0.1mM, EPS 0.1% and DMSO 1% had improved antitumor effects than paclitaxel alone.

IT 154889-68-6, KW-2189  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (micelle compns. containing exopolysaccharides from bacteria and pharmaceutically active agents)  
RN 154889-68-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 2 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2004:69153 CAPLUS  
DN 140:246406  
TI hnRNP L enhances sensitivity of the cells to KW-2189  
AU Taguchi, Fumiko; Kusaba, Hitoshi; Asai, Akira; Iwamoto, Yasuo; Yano, Keiichi; Nakano, Hirofumi; Mizukami, Tamio; Saijo, Nagahiro; Kato, Harubumi; Nishio, Kazuto  
CS Pharmacology Division, National Cancer Center Research Institute, Tokyo, Japan  
SO International Journal of Cancer (2003), Volume Date 2004, 108(5), 679-685  
CODEN: IJCNAA; ISSN: 0020-7136  
PB Wiley-Liss, Inc.  
DT Journal  
LA English  
AB Heterogeneous nuclear ribonucleoproteins (hnRNPs) are involved in several

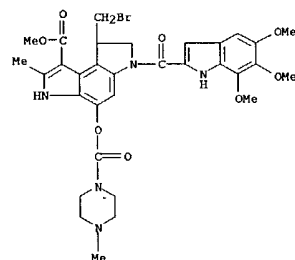
RNA-related biol. processes. We demonstrated hnRNP L as a candidate protein of DARP (duocarmycin-DNA adduct recognizing protein) by gel shift assay and amino acid sequencing. Stable transfectants of hnRNP L showed high sensitivity of the cells to the growth inhibitory effect of KW-2189, a duocarmycin derivative in vitro. Immunostaining of hnRNP L demonstrated differential intracellular localization of hnRNP L among human lung cancer cell lines. A transfection study using a series of deletion mutants of hnRNP L fused to indicate that the N-terminal portions of RRM(RNA recognition motif)1, RRM3 and RRM2 are involved in localization of hnRNP L. We identified sequences in these portions that have high homol.

with the sequences of known NLS (nuclear localization signal) and NES (nuclear export signal). hnRNP L is a factor that detcs. the sensitivities of cancer cells to the minor groove binder, and overexpression and differential intracellular localization of hnRNP L are involved in its function in lung cancer.

IT 148778-32-9  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (hnRNP L (duocarmycin-DNA adduct recognizing protein) enhances sensitivity of cells to KW-2189)  
RN 148778-32-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide (9CI)  
(CA INDEX NAME)

L14 ANSWER 2 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



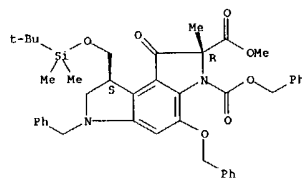
● HBr

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

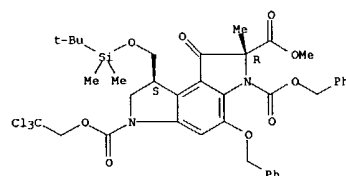
10/069,202

L14 ANSWER 3 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AN 2003:361118 CAPLUS  
 DN 139:85138  
 TI Total Synthesis of the Duocarmycins  
 AU Yamada, Ken; Kurokawa, Toshiaki; Tokuyama, Hidetoshi; Fukuyama, Tohru  
 CS Graduate School of Pharmaceutical Sciences, University of Tokyo, Bunkyo, Tokyo, 113-0033, Japan  
 SO Journal of the American Chemical Society (2003), 125(22), 6630-6631  
 CODEN: JACSAT; ISSN: 0002-7863  
 PB American Chemical Society  
 DT Journal  
 LA English  
 OS CASREACT 139:85138  
 AB The total synthesis of (+)-duocarmycin A and SA through a common indoline intermediate is described. The key reactions include selective lithiation of a 2,6-dibromiodobenzene derivative and diastereoselective addition to a chiral nitroalkene, copper-mediated aryl amination, and addition of aryllithium to oxalactones.  
 IT 556038-50-7P 556038-64-3P 556038-65-4P  
 556038-66-5P 556038-67-6P  
 RL: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of (+)-duocarmycin A and SA from a common indoline via selective lithiation, copper-mediated aryl amination, and diastereoselective addition)  
 RN 556038-50-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(2H)-dicarboxylic acid,  
 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,6,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-6-(phenylmethyl)-, 2-methyl 3-(phenylmethyl) ester, (2R,8S)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry. Rotation (+).

L14 ANSWER 3 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)

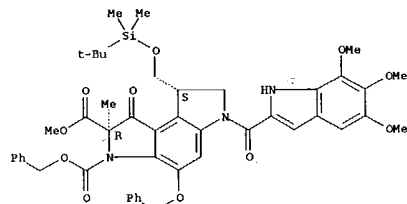


RN 556038-64-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,3,6-tricarboxylic acid,  
 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,2,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 3-(phenylmethyl) 6-(2,2,2-trichloroethyl) ester, (2R,8S)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry. Rotation (+).

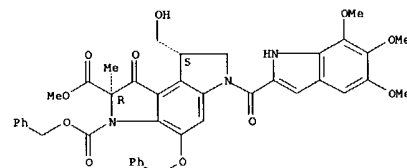


RN 556038-65-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(2H)-dicarboxylic acid,  
 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,6,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-methyl 3-(phenylmethyl) ester, (2R,8S)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry. Rotation (+).

L14 ANSWER 3 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)

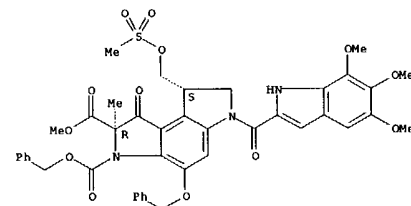


RN 556038-66-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(2H)-dicarboxylic acid,  
 1,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-methyl 3-(phenylmethyl) ester, (2R,8S)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry. Rotation (+).

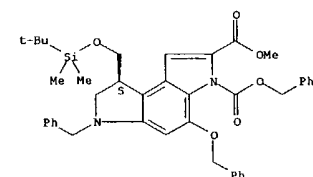


RN 556038-67-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(2H)-dicarboxylic acid,  
 1,6,7,8-tetrahydro-2-methyl-8-[[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-methyl 3-(phenylmethyl) ester, (2R,8S)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry. Rotation (+).

L14 ANSWER 3 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)



IT 556038-57-4P 556038-69-8P 556038-70-1P  
 556038-71-2P 556038-72-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of (+)-duocarmycin A and SA from a common indoline via selective lithiation, copper-mediated aryl amination, and diastereoselective addition)  
 RN 556038-57-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(6H)-dicarboxylic acid,  
 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-7,8-dihydro-4-(phenylmethoxy)-6-(phenylmethyl)-, 2-methyl 3-(phenylmethyl) ester, (8S)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry. Rotation (+).

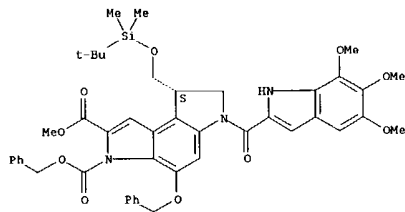


RN 556038-69-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(6H)-dicarboxylic acid,  
 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-7,8-dihydro-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-methyl 3-(phenylmethyl) ester, (8S)- (9CI) (CA INDEX NAME)

10/069,202

L14 ANSWER 3 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

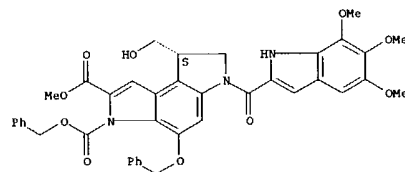
Absolute stereochemistry. Rotation (+).



RN 556038-70-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(6H)-dicarboxylic acid,

7,8-dihydro-8-[(hydroxymethyl)-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-methyl 3-(phenylmethyl) ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

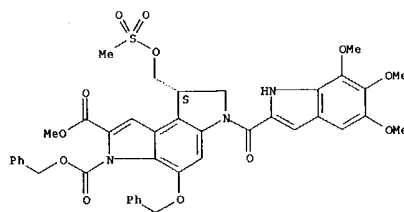


RN 556038-71-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(6H)-dicarboxylic acid,

7,8-dihydro-8-[[[(methylsulfonyl)oxy]methyl]-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-methyl 3-(phenylmethyl) ester, (8S)- (9CI) (CA INDEX NAME)

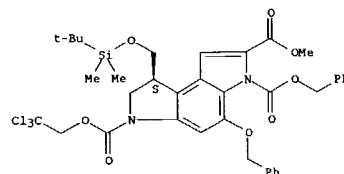
Absolute stereochemistry. Rotation (+).

L14 ANSWER 3 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 556038-72-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,3,6-tricarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-7,8-dihydro-4-(phenylmethoxy)-, 2-methyl 3-(phenylmethyl) 6-(2,2,2-trichloroethyl) ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2003:109220 CAPLUS  
DN 139:22032  
TI A concise and efficient synthesis of seco-duocarmycin SA  
AU Tietze, Lutz F.; Haunert, Frank; Feuerstein, Tim; Herzig, Tobias  
CS Institut für Organische Chemie der Georg August Universität  
Göttingen, 37077, Germany  
SO European Journal of Organic Chemistry (2003), (3), 562-566  
CODEN: EJOCFK; ISSN: 1434-193X  
PB Wiley-VCH Verlag GmbH & Co. KGaA  
DT Journal  
LA English  
OS CASREACT 139:22032  
AB A short and efficient synthesis of seco-duocarmycin SA

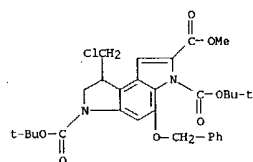
[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid Me ester], a highly potent cytostatic agent and direct precursor of the natural product duocarmycin SA, has been achieved. Starting from

available 2-methoxy-4-nitroaniline the synthetic protocol contains a Fischer indole synthesis to introduce the heterocyclic scaffold and a radical 5-exo-trig cyclization to furnish the (chloromethyl)indoline ring system as key reactions.

IT 539856-46-7P 539856-47-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

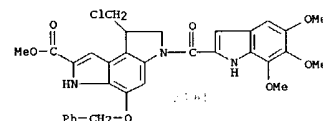
RACT (Reactant or reagent)  
(concise and efficient synthesis of seco-duocarmycin SA)

RN 539856-46-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,3,6-tricarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 3,6-bis(1,1-dimethylethyl) 2-methyl ester (9CI) (CA INDEX NAME)



RN 539856-47-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 4 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



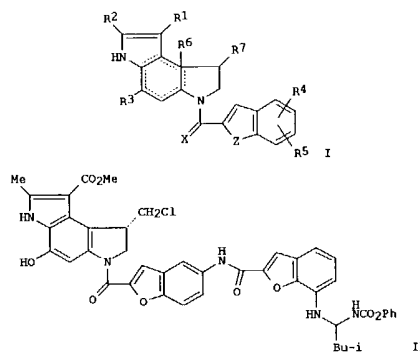
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/069,202

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AN 2002:927432 CAPLUS  
 DN 138:4470  
 TI Preparation of duocarmycin analogs as potent cytotoxins  
 IN Ng, Howard P.; McGee, Danny P. C.; Wu, Guoxian; Li, Zhihong; Gangwar, Sanjeev; Saunders, Oliver L.; Martichonok, Valeri; Astafieva, Irina; Moore, Jimmie; Yarranton, Geoffrey Thomas; King, David J.; Boyd, Sharon; Lobl, Thomas J.  
 PA Coulter Pharmaceutical, Inc., A Wholly Owned Subsidiary of Corixa Corporation, USA  
 SO PCT Int. Appl., 118 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002096910	A1	20021205	WO 2002-US17210	20020531
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003050331	A1	20030313	US 2002-160972	20020531
US 2003064984	A1	20030403	US 2002-161234	20020531
US 2003073852	A1	20030417	US 2002-161233	20020531
EP 1434778	A1	20040707	EP 2002-731994	20020531
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, NO, MK, CY, AL, TR				
PRAI US 2001-295196P	P	20010531		
US 2001-295259P	P	20010531		
US 2001-295342P	P	20010531		
US 2001-304908P	P	20010711		
WO 2002-US17210	W	20020531		
OS MARPAT 138:4470				
GI				

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)



AB Duocarmycin analogs I [X, Z = O, S, or imino; R1 = H, (un)substituted alkyl, carboxylic acid, ester, or amide; R2 = H, (un)substituted alkyl; R3 = -O, OH or derivative; R4, R5 = H, (un)substituted alkyl, (hetero)aryl, heterocycloalkyl, halo, NO2, NR15R16, NCOR15, O2CNR15R16, COO2R15, COR15, where R15 and R16 = H, (un)substituted (hetero)alkyl, (hetero)aryl, heterocycloalkyl, or peptidyl or NR15R16 = (un)substituted 4-6 membered heterocycloalkyl; R6 = a single bond; R7 = CH2-X, where X is a leaving group; or R6 and R7 may form a cyclopropyl ring] were prepared as potent cytotoxins. Peptidyl and disulfide linkers are cleaved in vivo. The linkers are of use in forming prodrugs and conjugates of the cytotoxins of the invention as well as other diagnostic and therapeutic moieties. Thus, compound II was prepared via acylation of the 5-amino-2-benzoyl intermediate.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)  
 Comps. I generally have an IC50 value in a proliferation assay of .apprx.

1-100 nM, preferably .apprx. 10-10 nM.

IT 477207-70-8P 477207-71-9P 477207-72-0P

477207-73-1P 477207-74-2P 477207-75-3P

477207-76-4P 477207-77-5P 477207-78-6P

477207-79-7P 477207-80-0P 477207-81-1P

477207-82-2P 477207-83-3P 477207-84-4P

477207-85-5P 477207-86-6P 477207-87-7P

477207-88-8P 477207-89-9P 477207-90-0P

477208-01-1P 477208-02-2P 477208-03-3P

477208-04-4P 477208-05-5P 477208-06-6P

477208-07-7P 477208-08-8P 477208-09-9P

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477208-22-2P 477208-23-3P 477208-24-4P

477208-25-5P 477208-26-6P 477208-27-7P

477208-28-8P 477208-29-9P 477208-30-0P

477208-31-1P 477208-32-2P 477208-33-3P

477208-34-4P 477208-35-5P 477208-36-6P

477208-37-7P 477208-38-8P 477208-39-9P

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477208-97-7P 477208-98-8P 477208-99-9P

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477209-54-4P 477209-55-5P 477209-56-6P

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)

477210-25-6P 477210-26-7P 477210-27-8P

477328-57-7P 477328-58-8P

RU: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

[prepn. of duocarmycin analogs as potent cytotoxins]

RN 477207-70-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,

8-(chloromethyl)-4-[[[(7S)-2-ethyl-1,11-dimethyl-7-(2-methylpropyl)-1,6,9-trioxo-10-oxa-2,5,8-triazadodec-1-yl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuran)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

MeO

CH2Cl

Me

Et

t-BuO

5

NH

HN

Me

MeO

CH2Cl

Me

Et

t-BuO

5

NH

HN

Me

MeO

CH2Cl

Me

Et

t-BuO

5

NH

HN

Me

MeO

CH2Cl

Me

Et

t-BuO

5

NH

HN

Me

MeO

CH2Cl

Me

Et

t-BuO

5

NH

HN

Me

MeO

CH2Cl

Me

Et

t-BuO

5

NH

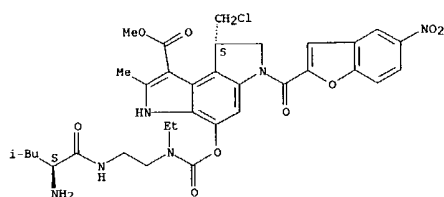
HN

Me



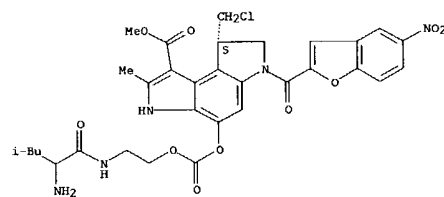
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L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477207-72-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
4-[[[2-[(2-amino-4-methyl-  
1-oxopentyl)amino]ethoxy]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-  
-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)-  
(9CI) (CA INDEX NAME)

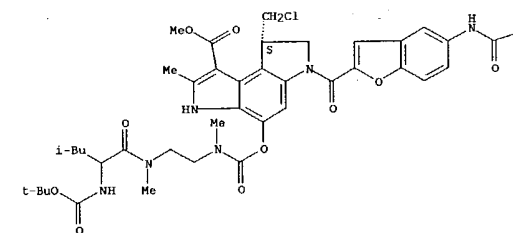
Absolute stereochemistry.



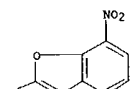
RN 477207-73-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[11,11-  
dimethyl-7-(2-methylpropyl)-1,6,9-trioxo-2,10-dioxo-5,8-diazadodec-1-  
yl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-,  
methyl ester, (8S)- (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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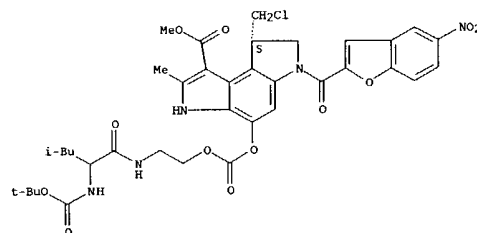


RN 477207-75-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
4-[[[2-[(2-amino-4-methyl-  
1-oxopentyl)methylamino]ethyl]methylamino]carbonyl]oxy]-8-(chloromethyl)-  
3,6,7,8-tetrahydro-2-methyl-6-[[[5-[[[7-nitro-2-  
benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester,  
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.

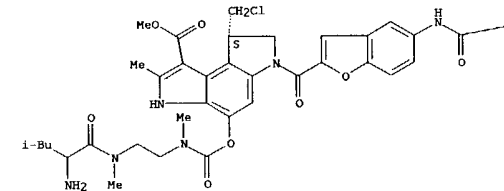


RN 477207-74-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-2-methyl-6-[[[5-[[[7-nitro-2-benzofuranyl]carbonyl]amino]-2-  
benzofuranyl]carbonyl]-4-[[[2,5,11,11-tetramethyl-7-(2-methylpropyl)-1,6,9-  
trioxo-10-oxa-2,5,8-triazadodec-1-yl]oxy]-, methyl ester, (8S)- (9CI)  
(CA INDEX NAME)

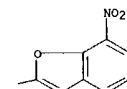
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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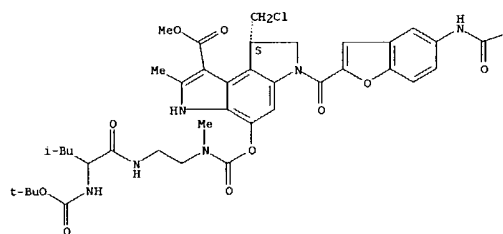
RN 477207-76-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-2-methyl-6-[[[5-[[[7-nitro-2-benzofuranyl]carbonyl]amino]-2-  
benzofuranyl]carbonyl]-4-[[[2,11,11-trimethyl-7-(2-methylpropyl)-1,6,9-  
trioxo-10-oxa-2,5,8-triazadodec-1-yl]oxy]-, methyl ester, (8S)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

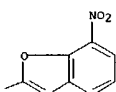
10/069,202

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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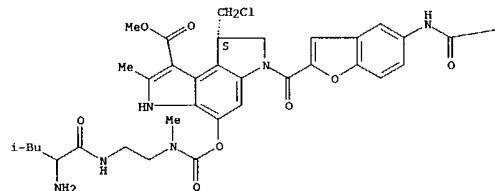
PAGE 1-B



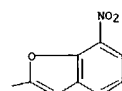
RN 477207-77-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
4-[[[2-[(2-amino-4-methyl-  
1-oxopentyl)amino]ethyl]methylamino]carbonyloxy]-8-(chloromethyl)-3,6,7,8-  
tetrahydro-2-methyl-6-[[5-[[[7-nitro-2-benzofuranyl]carbonyl]amino]-2-  
benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)  
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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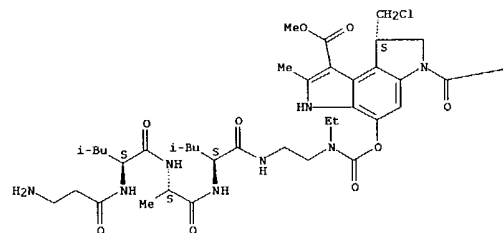
PAGE 1-B



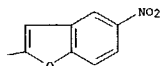
RN 477207-78-6 CAPLUS  
CN L-Leucinamide, β-alanyl-L-leucyl-L-alanyl-N-[2-[[[(8S)-8-(  
(chloromethyl)-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methyl-6-[[5-nitro-  
2-benzofuranyl]carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-  
yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)  
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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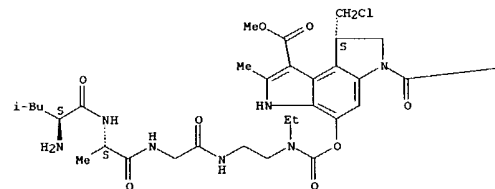
PAGE 1-B



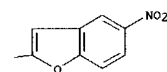
RN 477207-79-7 CAPLUS  
CN Glycinamide,  
L-leucyl-L-alanyl-N-[2-[[[(8S)-8-(chloromethyl)-3,6,7,8-  
tetrahydro-1-(methoxycarbonyl)-2-methyl-6-[[5-nitro-2-  
benzofuranyl]carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-  
yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)  
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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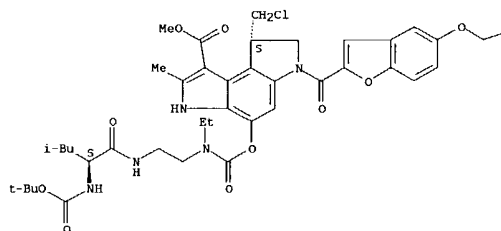


RN 477207-80-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-6-[[5-[2-(  
(dimethylamino)ethoxy)-2-benzofuranyl]carbonyl]-4-[[[(7S)-2-ethyl-11,11-  
dimethyl-7-(2-methylpropyl)-1,6,9-trioxo-10-oxa-2,5,8-triazadodec-1-  
yl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA  
INDEX NAME)  
Absolute stereochemistry.

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L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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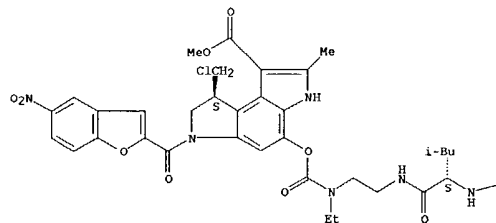


RN 477207-81-1 CAPLUS  
CN L-leucinamide,  
N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-  
L-alanyl-L-leucyl-N-[2-[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-1-  
(methoxycarbonyl)-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]benzo[1,2-  
b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA  
INDEX NAME)

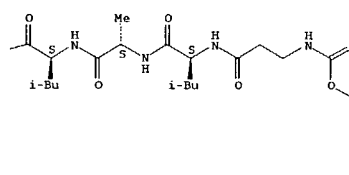
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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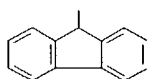


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L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

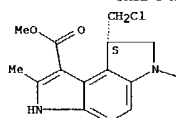
PAGE 2-B



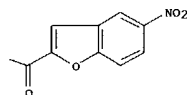
RN 477207-82-2 CAPLUS  
CN L-leucinamide, β-alanyl-L-leucyl-L-alanyl-L-leucyl-N-[2-[[[(8S)-8-  
(chloromethyl)-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methyl-6-[(5-nitro-  
2-benzofuranyl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-  
yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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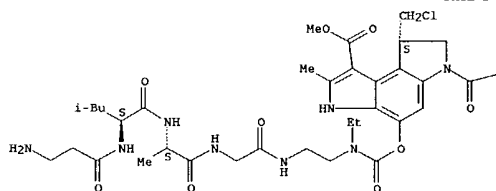
RN 477207-83-3 CAPLUS  
CN Glycinamide, β-alanyl-L-leucyl-L-alanyl-N-[2-[[[(8S)-8-

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

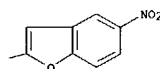
(chloromethyl)-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methyl-6-[(5-nitro-  
2-benzofuranyl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-  
yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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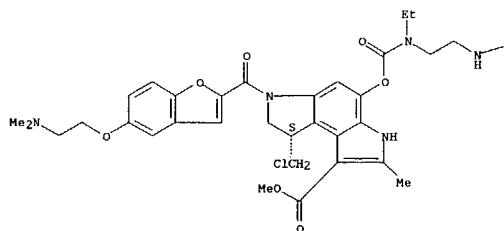
RN 477207-84-4 CAPLUS  
CN L-leucinamide,  
N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-  
L-alanyl-N-[2-[[[(8S)-8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-  
benzofuranyl)carbonyl]-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-  
methylbenzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

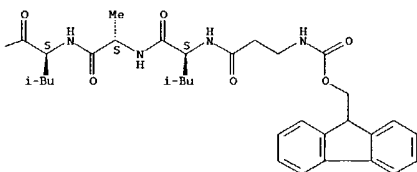
10/069,202

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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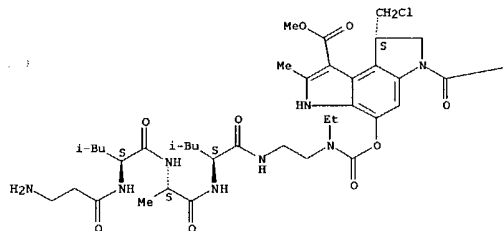
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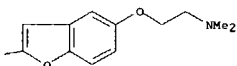
RN 477207-85-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
4-[[[2-[[[(2S)-2-amino-4-methyl-1-oxopentyl]amino]ethyl]ethylamino]carbonyl]oxy]-8-(chloromethyl)-6-  
[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)  
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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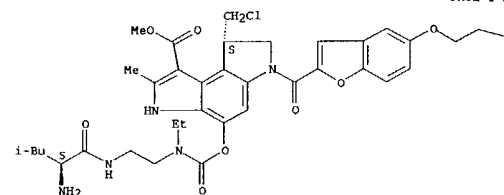
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RN 477207-87-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
4-[[[2-[[[(2S)-2-amino-4-methyl-1-oxopentyl]amino]ethyl]ethylamino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)  
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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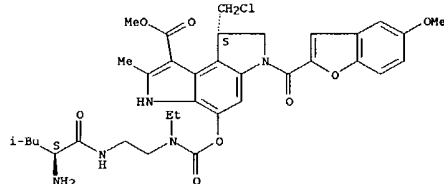


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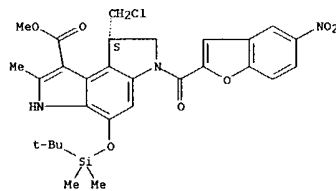
NMe2

RN 477207-86-6 CAPLUS  
CN L-Leucinamide, β-alanyl-L-leucyl-L-alanyl-N-[2-[[[(8S)-8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methylbenzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)  
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



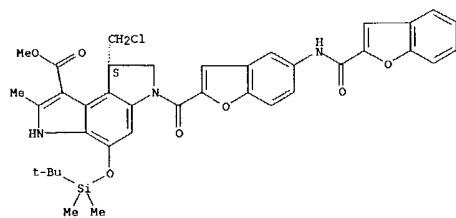
RN 477207-96-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[5-nitro-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)  
Absolute stereochemistry.



RN 477207-97-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[2-benzofuranyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)  
Absolute stereochemistry.

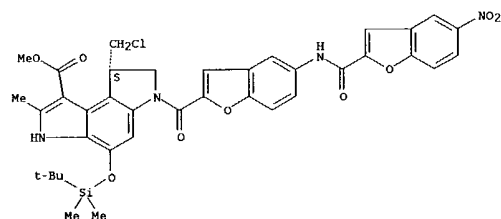
10/069,202

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



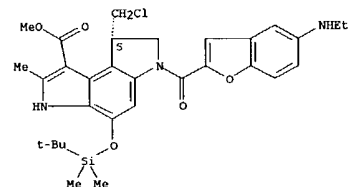
RN 477207-99-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[[(5-nitro-2-benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



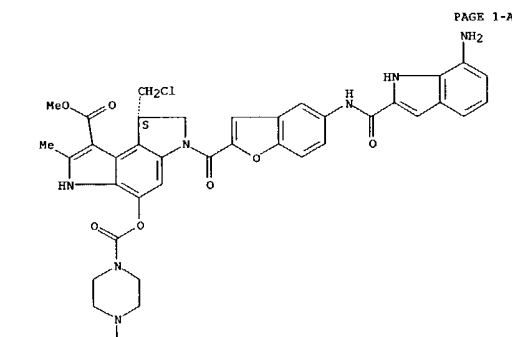
RN 477208-00-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[[(5-amino-2-benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477208-10-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[[(5-amino-1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

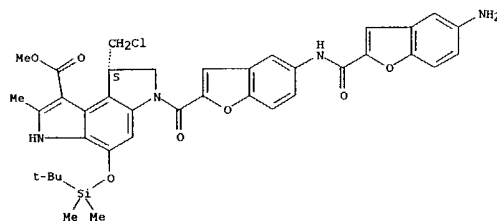
Absolute stereochemistry.



PAGE 1-A

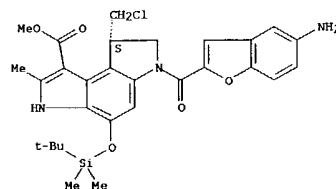
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.



RN 477208-05-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[[(5-amino-2-benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477208-07-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-[[[(5-ethylamino)-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

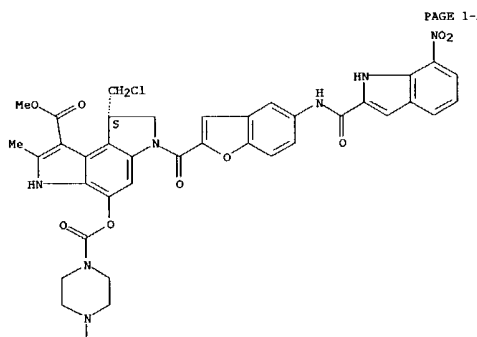
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued) PAGE 2-A



RN 477208-12-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[[[(7-nitro-1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



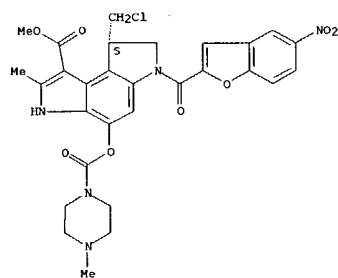
PAGE 1-A

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RN 477208-13-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[[[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

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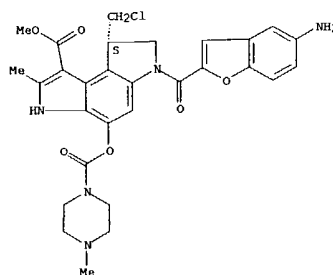
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
Absolute stereochemistry.



RN 477208-14-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[(5-amino-2-benzofuranyl)carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

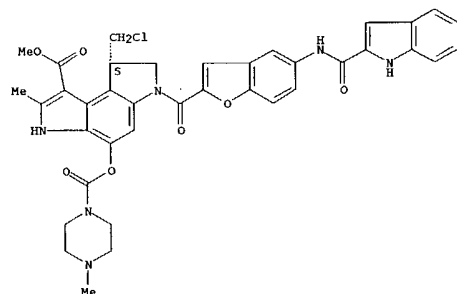
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477208-18-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[5-[(1H-indol-2-ylcarbonyl)amino]-2-benzofuranyl)carbonyl]-2-methyl-4-[[4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

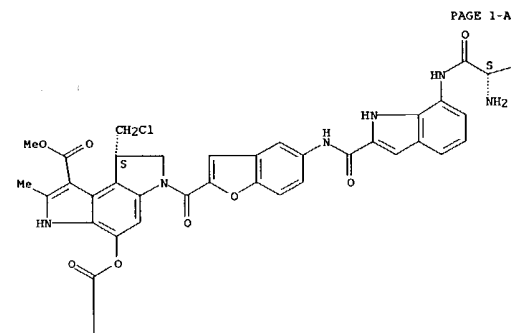
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477208-21-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[7-[[[2S]-2-amino-4-methyl-1-oxopentyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

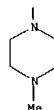


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PAGE 2-A

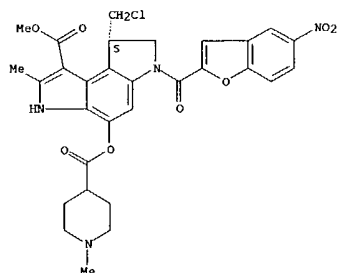


RN 477208-24-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[4-methyl-1-piperidinyl)carbonyl]oxy]-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/069,202

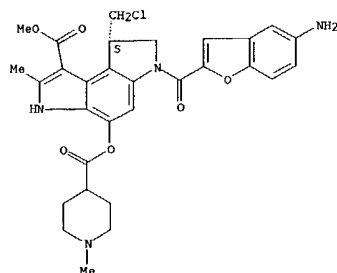
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477208-25-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[(5-amino-2-benzofuranyl)carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(1-methyl-4-piperidinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

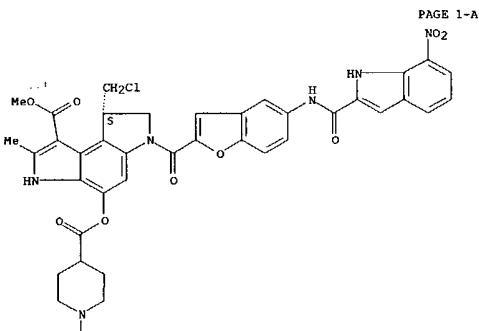
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477208-26-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(1-methyl-4-piperidinyl)carbonyl]oxy]-6-[[[(7-nitro-1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

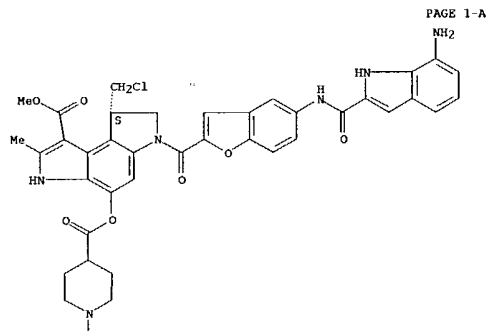


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RN 477208-27-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[[5-[[[(7-amino-1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(1-methyl-4-piperidinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

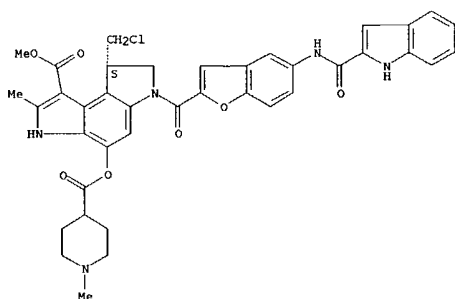


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RN 477208-28-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[[5-[[[(1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-2-methyl-4-[[[(1-methyl-4-piperidinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

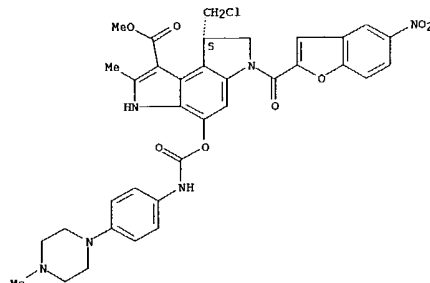
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477208-34-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-3,6,7,8-  
 tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)phenyl]amino]carbonyl]  
 oxy]-6-[[5-nitro-2-benzofuranyl]carbonyl]-, methyl ester, (8S)-  
 (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

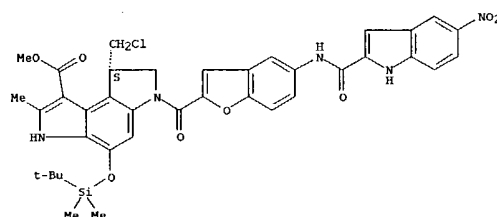


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RN  477208-39-2  CAPLUS
CN  Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
    8-(chloromethyl)-4-[[{1,1-
dimethylethyl}dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[5-[[{5-
nitro-1H-indol-1-yl}carbonyl]amino]-2-benzofuranyl]carbonyl], methyl
ester. (8S)- (9CI) (CA INDEX NAME)

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Absolute stereochemistry.

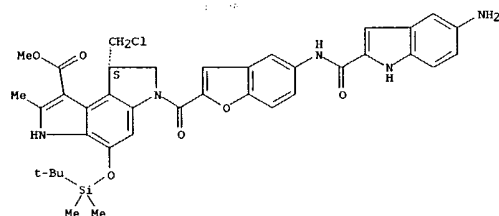


RN 477208-40-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
6-[[5-[[5-amino-1H-indol-

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

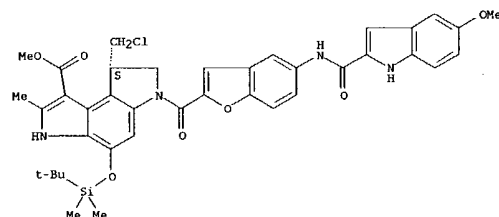
2-yl) carbonyl] amino]-2-benzofuranyl] carbonyl]-8-(chloromethyl)-4-[[1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

**Absolute stereochemistry.**



RN 477208-43-8 CASIUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[1,1-  
dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-6-[[5-[[[5-methoxy-1H-  
indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-2-methyl-, methyl  
ester, (8S)- (9CI) (CA INDEX NAME)

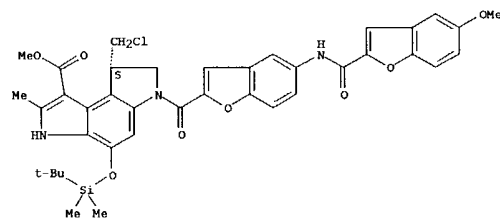
**Absolute stereochemistry.**



RN 477208-44-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-4-[[[1,1-  
 dimethylethyl)dimethylsilyloxy]-3,6,7,8-tetrahydro-6-[[5-[(5-methoxy-2-

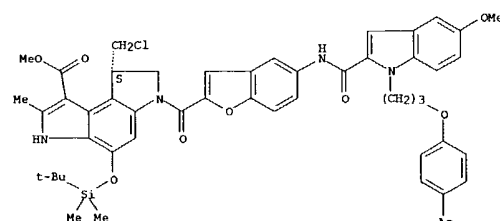
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-2-methyl-,  
methyl  
ester. (8S)- (9CI) (CA INDEX NAME)

**Absolute stereochemistry.**



RN 477208-45-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[1-[3-(4-acetylphenoxy)propyl]-5-methoxy-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

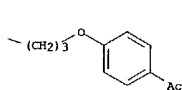
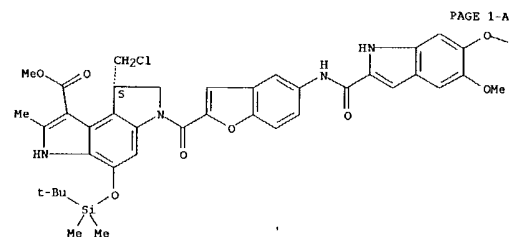


RN 477208-46-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[6-[3-(4-acetylphenoxy)propoxy]-5-methoxy-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)



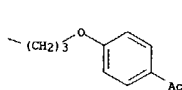
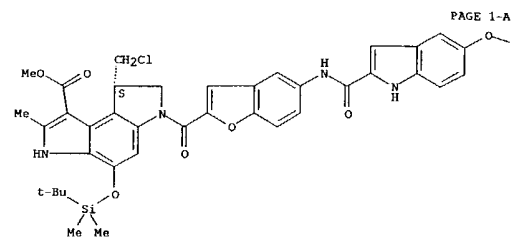
10/069,202

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
Absolute stereochemistry.



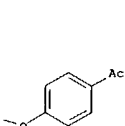
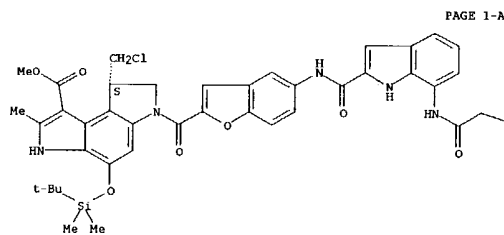
RN 477208-47-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[5-[3-(4-acetylphenoxy)propoxy]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)  
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



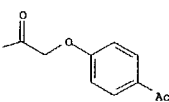
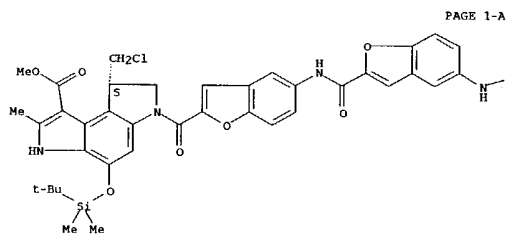
RN 477208-48-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[7-[[[4-(acetylphenoxy)acetyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)  
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477208-49-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[5-[[[4-(acetylphenoxy)acetyl]amino]-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)  
Absolute stereochemistry.

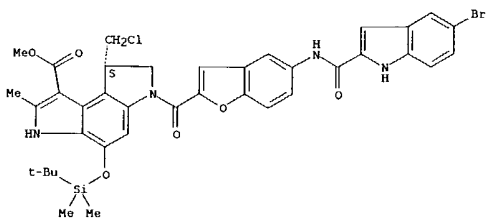
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477208-50-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[5-bromo-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)  
Absolute stereochemistry.

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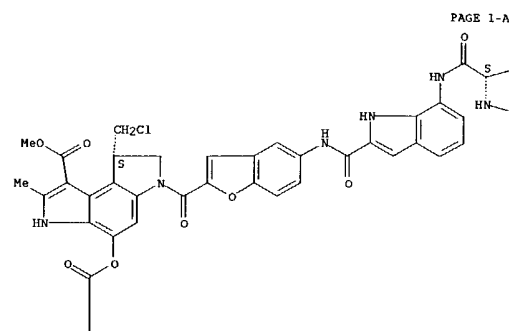
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



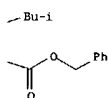
RN 477208-51-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-3,6,7,8-  
 tetrahydro-2-methyl-6-[[[5-[[[7-[[[(2S)-4-methyl-1-oxo-2-  
 [[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1H-indol-2-  
 yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-4-[[[4-methyl-1-  
 piperazinyl]carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX  
 NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

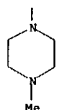


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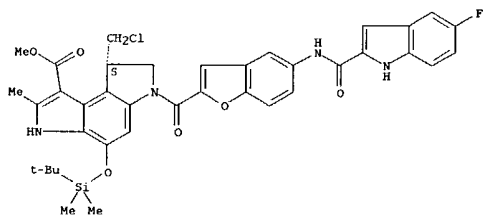
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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RN 477208-52-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-4-[[[(1,1-  
 dimethylethyl)dimethylsilyl]oxy]-6-[[[5-[[[(5-fluoro-1H-indol-2-  
 yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-  
 methyl ester, (8S)- (9CI) (CA INDEX NAME)

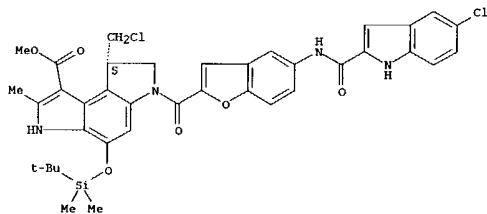
Absolute stereochemistry.



RN 477208-53-0 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 6-[[[5-[[[(5-chloro-1H-indol-  
 2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[(1,1-  
 dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl  
 ester, (8S)- (9CI) (CA INDEX NAME)

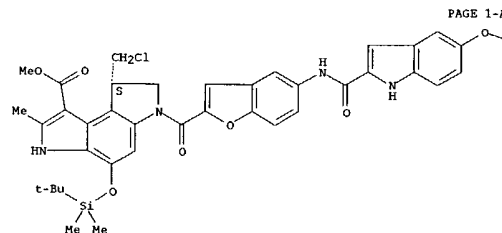
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477208-54-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-4-[[[(1,1-  
 dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[[5-[[[5-  
 (trifluoromethoxy)-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-  
 methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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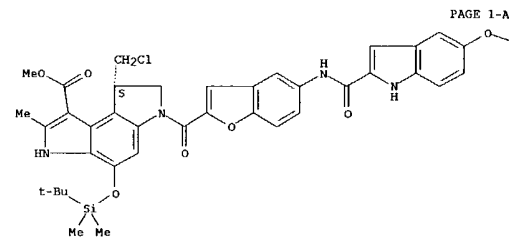
RN 477208-56-3 CAPLUS

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L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[[5-[[[5-(phenylmethoxy)-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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RN 477208-57-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[[5-[[[5-(phenylmethoxy)-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

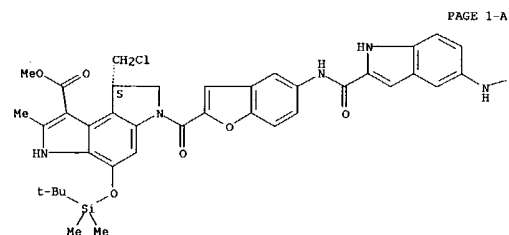
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
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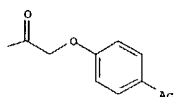


RN 477208-60-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[[5-[[[5-[[[4-acetylphenoxy]acetyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

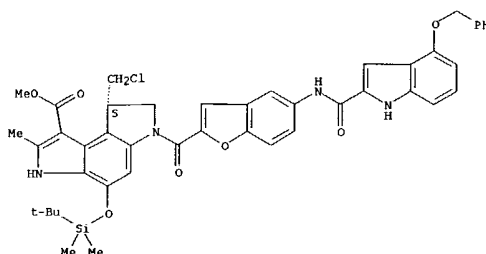


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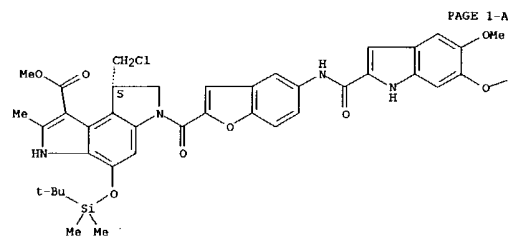
RN 477208-61-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
6-[[[5-[[[5-[[[3-(4-acetylphenoxy)propyl]dithio]-2-methyl-1-oxopropyl]amino]-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



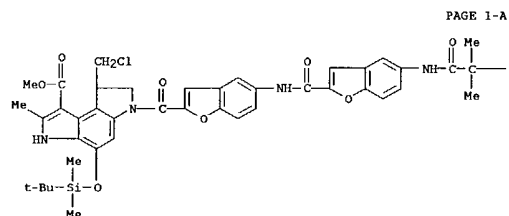
RN 477208-58-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-6-[[[5-[[[5-methoxy-6-(phenylmethoxy)-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

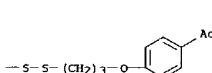


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L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
[[[1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



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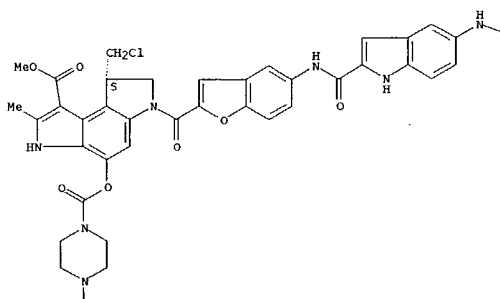
RN 477208-62-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
6-[[[5-[[[5-[[[2S]-2-amino-4-methyl-1-oxopentyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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PAGE 1-B

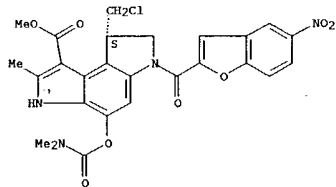


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RN 477208-63-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[methylamino]carbonyl]oxy]-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

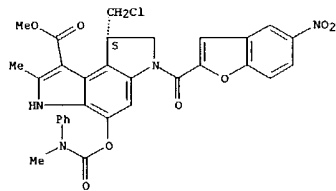
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



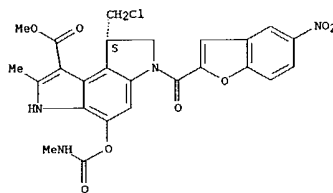
RN 477208-70-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[methylphenylamino]carbonyl]oxy]-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



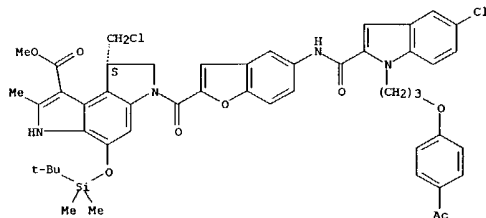
RN 477208-71-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[[5-[(7-nitro-2-benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477208-65-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[[5-[[[1,3-(4-acetylphenoxy)propyl]-5-chloro-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

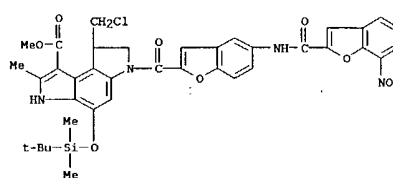
Absolute stereochemistry.



RN 477208-69-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

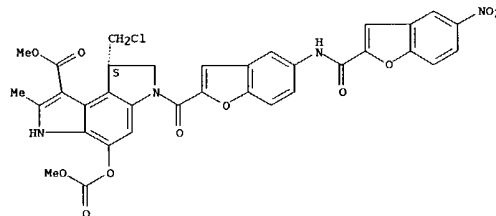
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



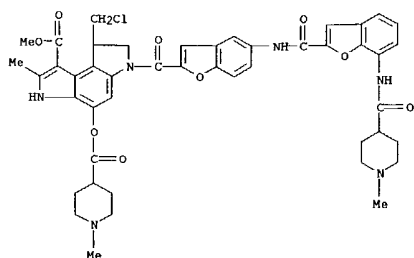
RN 477208-75-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[methoxycarbonyl]oxy]-6-[[[5-[(7-nitro-2-benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



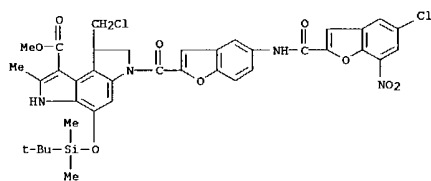
RN 477208-79-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[[[5-[[[7-[(1-methyl-4-piperidinyl)carbonyl]amino]-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-4-[[[(1-methyl-4-piperidinyl)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



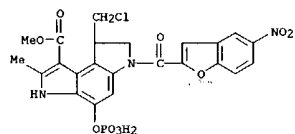
RN 477208-84-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-6-[[5-  
 [[5-(5-chloro-7-nitro-2-benzofuranyl)carbonyl]amino]-2-

benzofuranyl carbonyl]-4-[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-  
 tetrahydro-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



RN 477208-88-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[bis(1,1-  
 dimethylethoxy)phosphinyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-  
 methyl-6-[[5-(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester (9CI) (CA  
 INDEX NAME)

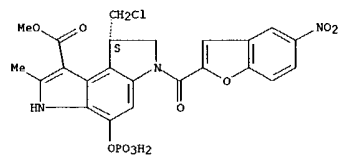
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477208-91-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-3,6,7,8-

tetrahydro-2-methyl-6-[[5-(5-nitro-2-benzofuranyl)carbonyl]-4-(phosphonoxy)-  
 , 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

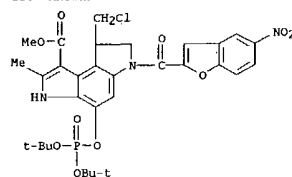
Absolute stereochemistry.



RN 477208-94-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[7-amino-2-  
 benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-  
 [[2,5-dioxo-1-pyrrolidinyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl  
 ester, (8S)- (9CI) (CA INDEX NAME)

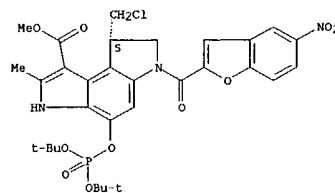
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477208-89-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[bis(1,1-  
 dimethylethoxy)phosphinyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-  
 methyl-6-[[5-(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)-  
 (9CI) (CA INDEX NAME)

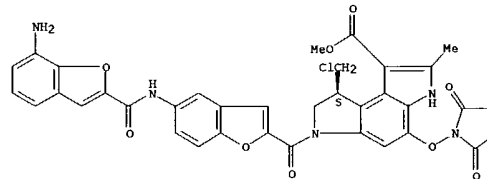
Absolute stereochemistry.



RN 477208-90-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-3,6,7,8-

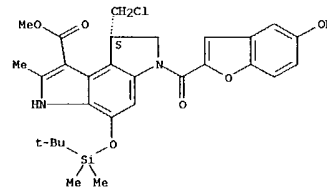
tetrahydro-2-methyl-6-[[5-(5-nitro-2-benzofuranyl)carbonyl]-4-(phosphonoxy)-  
 , 1-methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



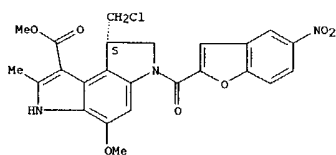
RN 477209-15-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-4-[[1,1-  
 dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-6-[[5-(5-hydroxy-2-  
 benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX  
 NAME)

Absolute stereochemistry.



RN 477209-20-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-3,6,7,8-  
 tetrahydro-4-methoxy-2-methyl-6-[[5-(5-nitro-2-benzofuranyl)carbonyl]-,  
 methyl ester, (8S)- (9CI) (CA INDEX NAME)

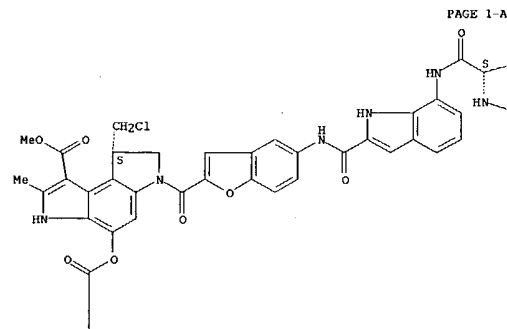
Absolute stereochemistry.



RN 477209-21-5 CAPLUS

CN L-Leucinamide,  $\beta$ -alanine-L-leucyl-L-alanyl-N-[2-[[[2-[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[4-methyl-1-piperazinyl]carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrole-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

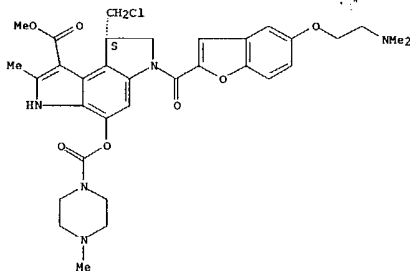
Absolute stereochemistry.



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L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

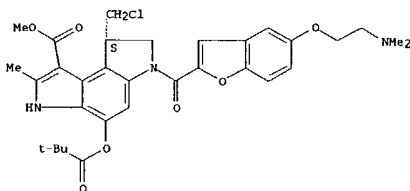
Absolute stereochemistry.



RN 477209-25-9 CAPLUS

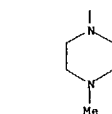
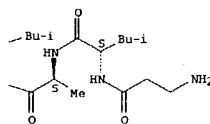
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-4-[(2,2-dimethyl-1-oxopropoxy)-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477209-26-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-

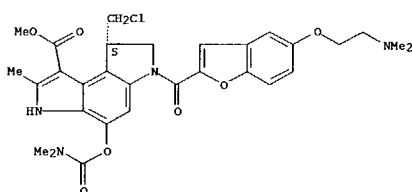


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RN 477209-23-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[dimethylamino]carbonyl]oxy]-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

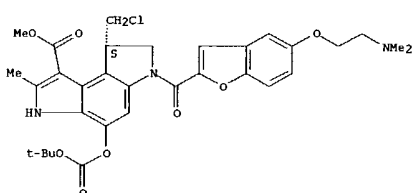


RN 477209-24-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-4-[[[1,1-dimethylethoxy]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

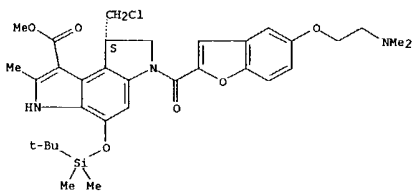
Absolute stereochemistry.



RN 477209-27-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-4-[[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



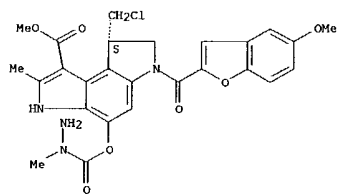
RN 477209-28-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[5-methoxy-2-benzofuranyl]carbonyl]-2-methyl-4-[[[1-methylhydrazino]carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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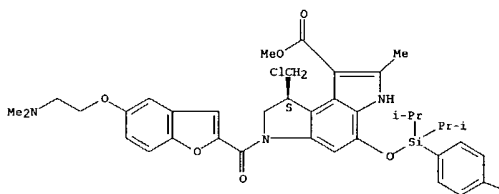
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-32-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-4-[[4-(methoxymethoxy)phenyl]bis[(1-methylethyl)silyl]oxy]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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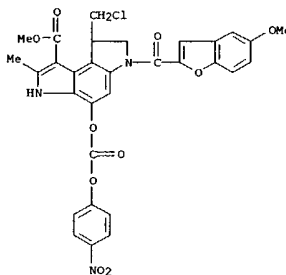


L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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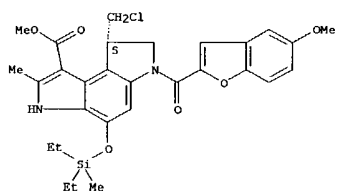
RN 477209-33-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-4-[[4-(methoxymethoxy)phenyl]bis[(1-methylethyl)silyl]oxy]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)



RN 477209-34-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-4-[[4-(methoxymethoxy)phenyl]bis[(1-methylethyl)silyl]oxy]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

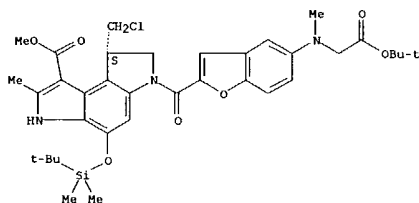
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.



RN 477209-35-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-4-[[4-(methoxymethoxy)phenyl]bis[(1-methylethyl)silyl]oxy]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

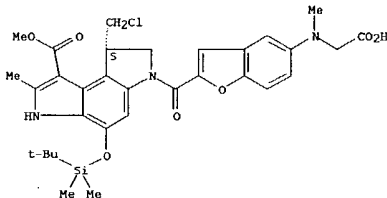
Absolute stereochemistry.



RN 477209-36-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[4-(methoxymethoxy)phenyl]bis[(1-methylethyl)silyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

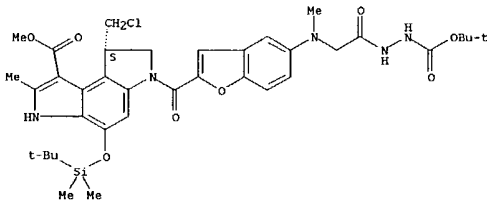
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-37-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-4-[[4-(methoxymethoxy)phenyl]bis[(1-methylethyl)silyl]oxy]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

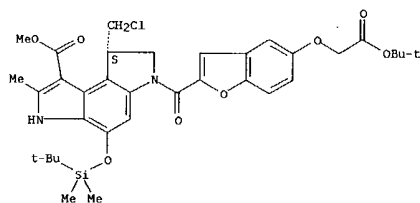


RN 477209-38-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-4-[[4-(methoxymethoxy)phenyl]bis[(1-methylethyl)silyl]oxy]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

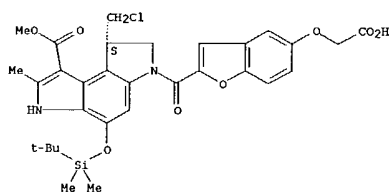
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L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-39-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
6-[[5-(carboxymethoxy)-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-,  
1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

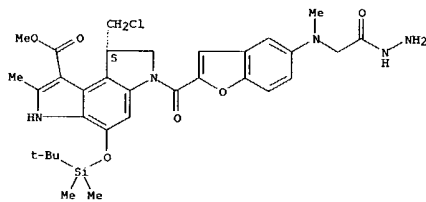
Absolute stereochemistry.



RN 477209-40-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-6-[[5-[2-[[2-[(1,1-dimethylethoxy)carbonyl]hydrazino]-2-oxoethoxy]-2-benzofuranyl]carbonyl]-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

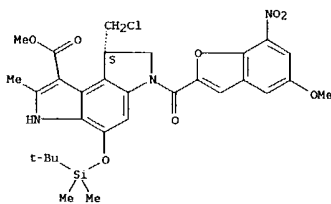
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-43-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-6-[(5-methoxy-7-nitro-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

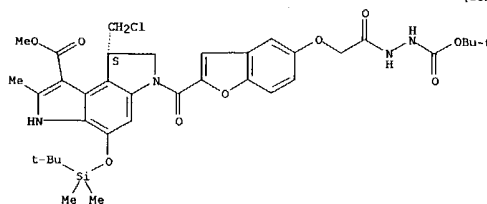
Absolute stereochemistry.



RN 477209-44-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
6-[[7-amino-5-methoxy-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

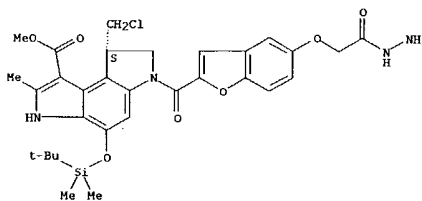
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-41-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-[[5-(2-hydrazino-2-oxoethoxy)-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

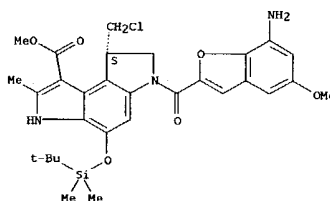
Absolute stereochemistry.



RN 477209-42-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-[[5-[(2-hydrazino-2-oxoethyl)methylamino]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

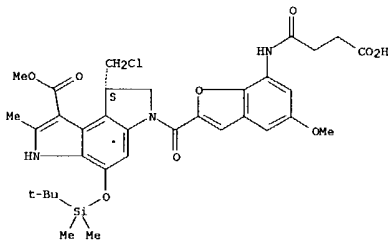
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-45-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[7-[(3-carboxy-1-oxopropoxy)amino]-5-methoxy-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

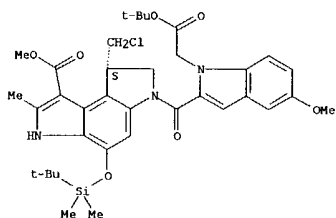


RN 477209-47-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-6-[[[1-[2-(1,1-dimethylethoxy)-2-oxoethyl]-5-methoxy-1H-indol-2-yl]carbonyl]-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

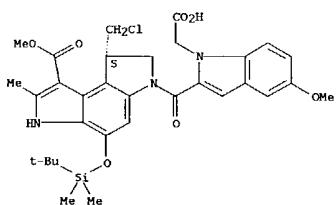


L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-48-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 6-[[1-(carboxymethyl)-5-methoxy-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-4-[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-,  
 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477209-49-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-6-[[1,1-dimethylethoxy]carbonyl]hydrazino]-2-oxoethyl]-5-methoxy-1H-indol-2-yl]carbonyl]-4-[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

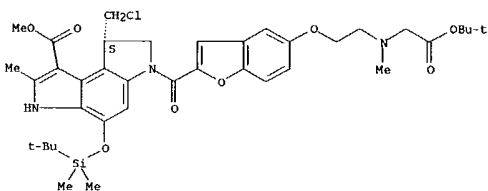
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RN 477209-51-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-6-[[1,1-dimethylethoxy]-2-oxoethyl]methylamino]ethoxy]-2-benzofuranyl]carbonyl]-4-[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

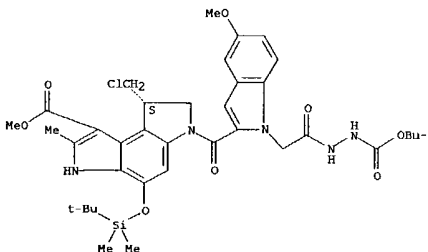


RN 477209-52-2 CAPLUS  
 CN L-Leucinamide,  
 N-[1,4-dioxo-4-(phenylmethoxy)butyl]-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[1,1-dimethylethyl]dimethylsilyl]oxy]-1,6-dihydro-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

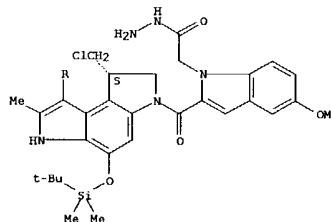
Absolute stereochemistry.



RN 477209-50-0 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-4-[[1,1-dimethylethyl]dimethylsilyl]oxy]-6-[[1-(2-hydrazino-2-oxoethyl)-5-methoxy-1H-indol-2-yl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

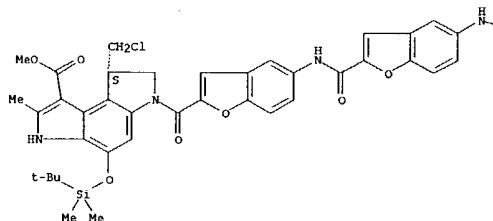
Absolute stereochemistry.

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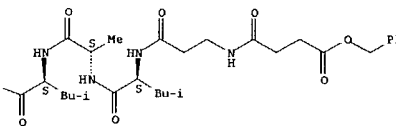


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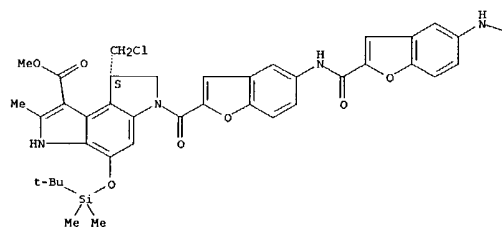
RN 477209-54-4 CAPLUS  
 CN L-Leucinamide,  
 N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[1,1-dimethylethyl]dimethylsilyl]oxy]-1,6-dihydro-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

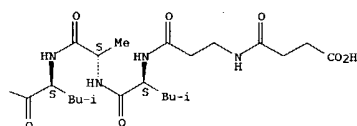
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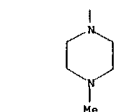
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RN 477209-59-9 CAPLUS  
CN L-Leucinamide,  
N-(5-carboxy-1-oxopentyl)- $\beta$ -alanyl-L-leucyl-L-alanyl-N-  
[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-  
[[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-  
yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI)  
(CA INDEX NAME)

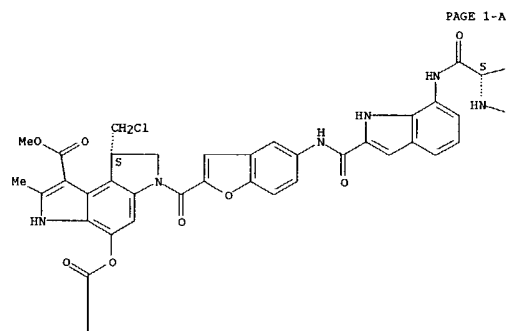
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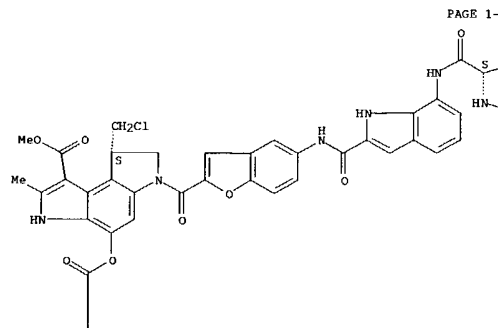
RN 477209-60-2 CAPLUS  
CN L-Leucinamide, N-(6-methoxy-1,6-dioxohexyl)- $\beta$ -alanyl-L-leucyl-L-  
alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-  
methyl-5-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-  
b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-  
yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

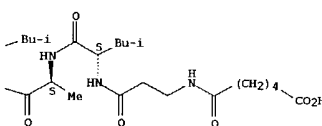


L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
Absolute stereochemistry.

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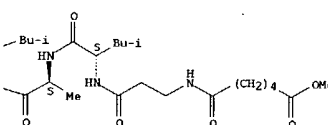


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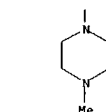


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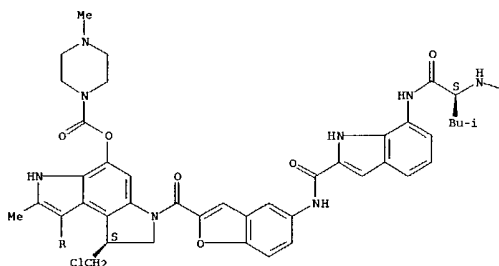
RN 477209-61-3 CAPLUS  
CN L-Leucinamide,  
N-[(9H-fluoren-9-ylmethoxy)carbonyl]- $\beta$ -alanyl-L-leucyl-  
L-alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-  
7-methyl-5-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-  
b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-  
yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

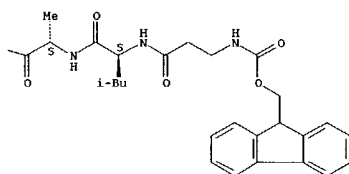
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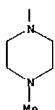


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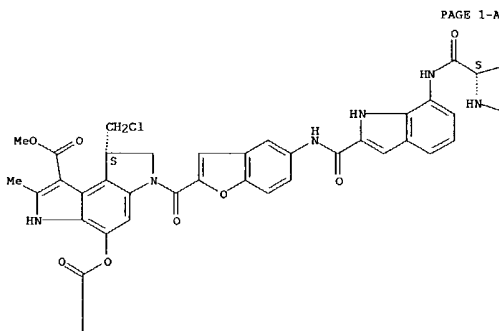
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RN 477209-63-5 CAPLUS  
CN L-Leucinamide,  
N-[1,4-dioxo-4-(phenylmethoxy)butyl]-β-alanyl-L-leucyl-  
L-alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-  
7-methyl-5-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-  
b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-  
yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

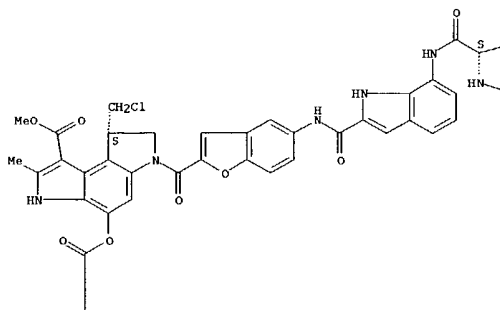


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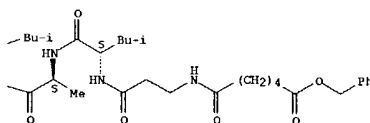
RN 477209-62-4 CAPLUS  
CN L-Leucinamide,  
N-[1,6-dioxo-6-(phenylmethoxy)hexyl]-β-alanyl-L-leucyl-  
L-alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-  
7-methyl-5-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-  
b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-  
yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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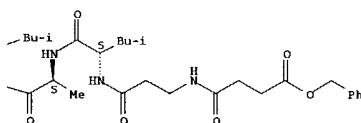


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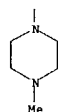


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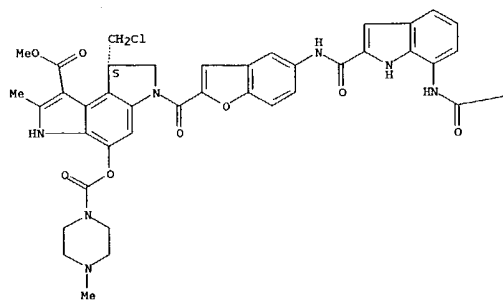
RN 477209-65-7 CAPLUS  
CN L-Leucinamide,  
N-[3-(2,5-dioxo-1-pyrrolidinyl)-1-oxopropyl]-L-leucyl-L-  
alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-  
methyl-5-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-  
b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-  
yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

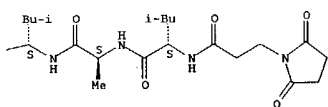
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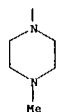
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RN 477209-66-8 CAPLUS  
CN L-Leucinamide,  
N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[4-methyl-1-piperazinyl]carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)  
(CA)

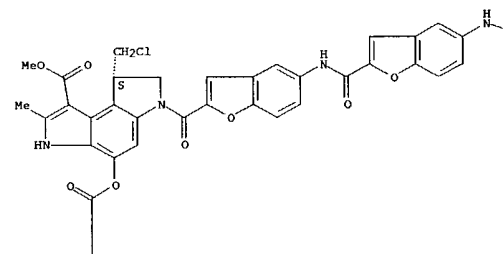
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RN 477209-69-1 CAPLUS  
CN L-Leucinamide, β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[4-methyl-1-piperazinyl]carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)  
Absolute stereochemistry.

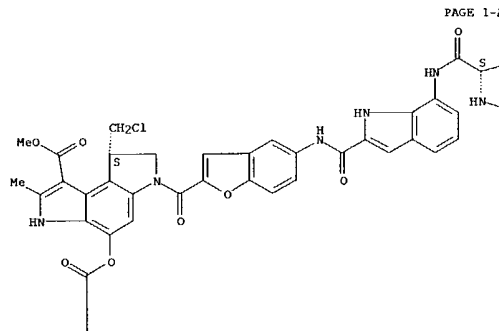
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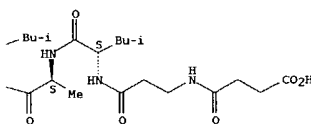
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
INDEX NAME)

Absolute stereochemistry.

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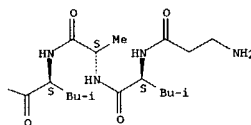


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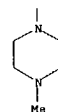


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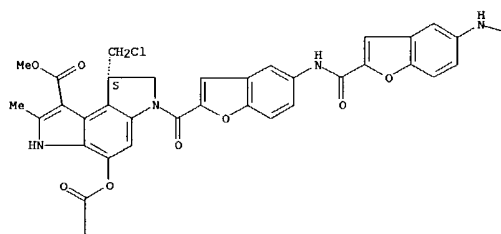


RN 477209-70-4 CAPLUS  
CN L-Isoleucinamide, β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[4-methyl-1-piperazinyl]carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)  
Absolute stereochemistry.

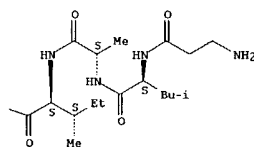
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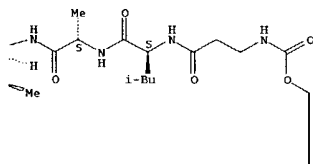


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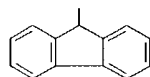


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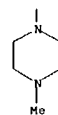


RN 477209-75-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[[5-[[[7-[[[25,35]-2-amino-3-methyl-1-oxopentyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[1-methyl-4-piperidinyl]carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

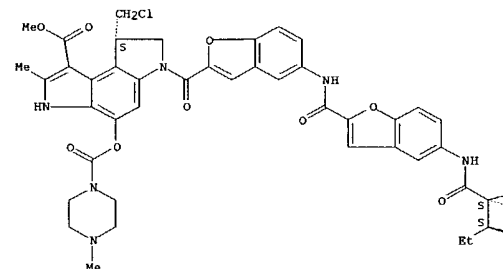
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RN 477209-71-5 CAPLUS  
CN L-Isoleucinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[1S]-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[[4-methyl-1-piperazinyl]carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrole-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

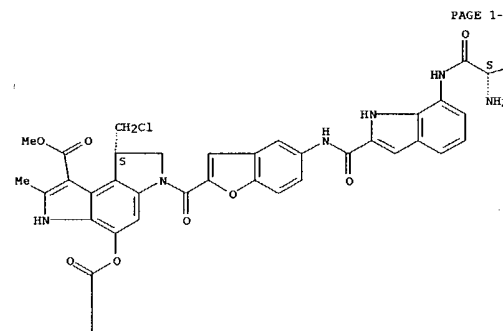
Absolute stereochemistry.

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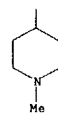
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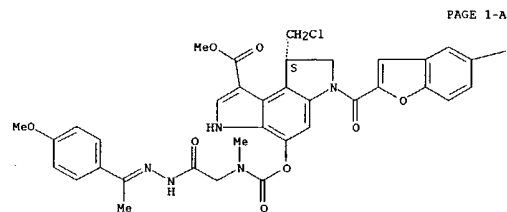
PAGE 2-A



RN 477209-76-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[2-[[[1-(4-methoxyphenyl)ethylidene]hydrazino]-2-oxoethyl]methylamino]carbonyl]oxy]-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

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L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
Absolute stereochemistry.  
Double bond geometry unknown.



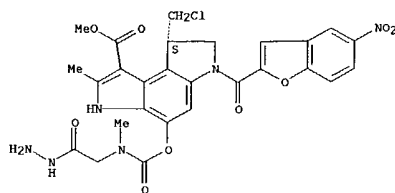
PAGE 1-B

—NO<sub>2</sub>

RN 477209-77-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[2-  
hydrazino-2-oxoethyl)methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl  
6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA  
INDEX NAME)

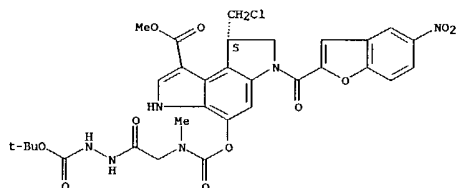
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-78-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[2-  
[2-[(1,1-dimethylethoxy)carbonyl]hydrazino]-2-  
oxoethyl)methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5-nitro-2-  
benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

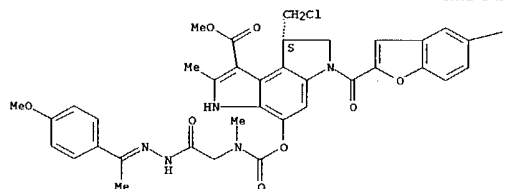


RN 477209-79-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-4-[[[2-[[1-(4-methoxyphenyl)ethylidene]hydrazino]-2-  
oxoethyl)methylamino]carbonyl]oxy]-2-methyl-6-[(5-nitro-2-  
benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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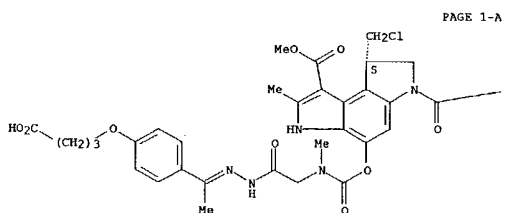


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—NO<sub>2</sub>

RN 477209-80-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[[1-(4-(3-  
carboxypropoxy)phenyl)ethylidene]hydrazino]-2-  
oxoethyl)methylamino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-  
[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)-  
(9CI) (CA INDEX NAME)

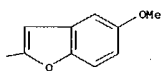
Absolute stereochemistry.  
Double bond geometry unknown.



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L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

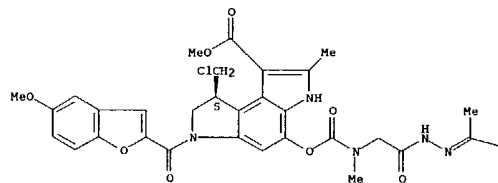
PAGE 1-B



RN 477209-81-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[2-  
[[1-(4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutoxy)phenyl]ethylidene]hy  
drazino]-2-oxoethyl)methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5-  
methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.

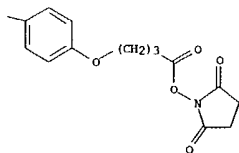
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L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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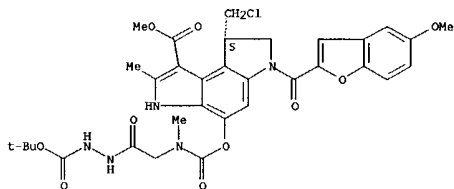


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RUN 477209-82-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[[2-
[2-[(1,1-dimethylethoxy)carbonyl]hydrazino]-2-
oxoethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[[5-methoxy-2-
benzofuranyl]carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA
INDEX
NAME)

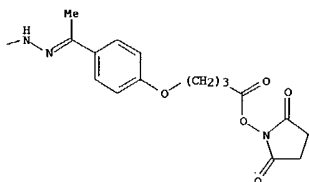
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**Absolute stereochemistry.**



L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

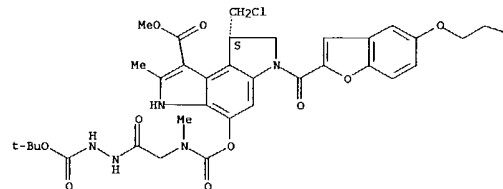
PAGE 1-B



RN 477209-84-0 CAPLUS  
 CN Benz[1,2-b:4,3-b']dipyrole-1-carboxylic acid,  
 8-(chloromethyl)-6-[[5-[2-  
 (dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-4-[[[2-[2-[(1,1-  
 dimethylethoxy)carbonyl]hydrazino]-2-oxoethyl)methylamino]carbonyl]oxy]-  
 3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX  
 NAME)

**Absolute stereochemistry.**

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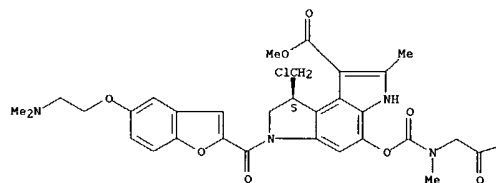
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 477209-83-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-6-[[5-[2-

(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-4-[[[2-[[1-[4-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutoxy]phenyl]ethylidene]hydrazino]-2-oxoethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.

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L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

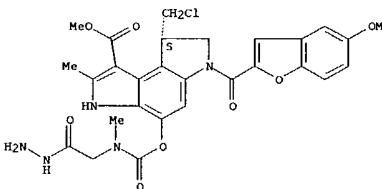
PAGE 1-B



RN 477209-85-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[(2-

hydrazino-2-oxoethyl)methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)-(9CI)  
(CA  
INDEX NAME)

**Absolute stereochemistry.**



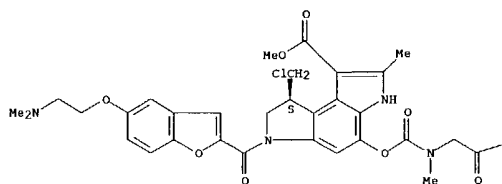
CN 477209-86-2 CAPLUS  
 CN Benzo[1,2-b;4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-4-[[[2-  
 [[1-[4-[4-{[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)propyl]amino]-4-  
 oxobutoxyl]phenyl]ethylidene]hydrazino]-2-oxoethyl]methylamino]carbonyloxy]  
 -6-[5-[[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbamoyl]-3,6,7,8-  
 tetrahydro-2-methyl-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.

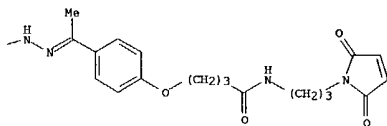
10/069,202

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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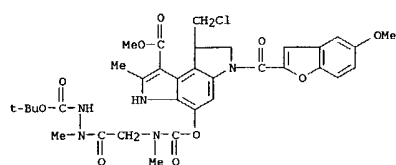


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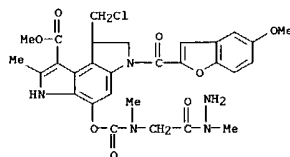


RN 477209-87-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[2-  
[2-[(1,1-dimethylethoxy)carbonyl]-1-methylhydrazino]-2-  
oxoethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5-methoxy-2-  
benzofuranyl)carbonyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-88-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-4-[[[methyl[2-  
(1-methylhydrazino)-2-oxoethyl]amino]carbonyl]oxy]-, methyl ester  
(9CI) (CA INDEX NAME)

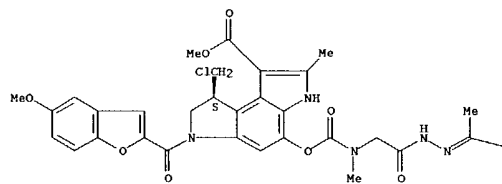


RN 477209-89-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[2-  
[[1-[4-[4-[(3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)propyl]amino]-4-  
oxobutoxy]phenyl]ethylidene]hydrazino]-2-oxoethyl]methylamino]carbonyl]oxy  
]-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-,  
methyl ester, (8S)- (9CI) (CA INDEX NAME)

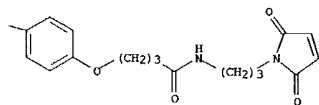
Absolute stereochemistry.  
Double bond geometry unknown.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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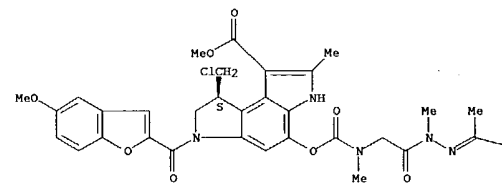


RN 477209-90-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[2-  
[[1-[4-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutoxy]phenyl]ethylidene]me  
thylhydrazino]-2-oxoethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-  
[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)-  
(9CI) (CA INDEX NAME)

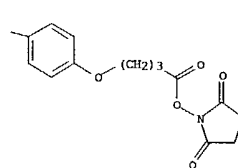
Absolute stereochemistry.  
Double bond geometry unknown.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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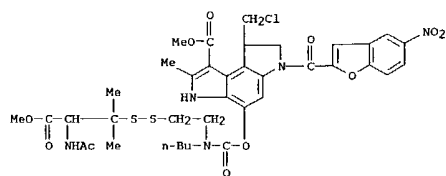


RN 477209-91-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
4-[[[2-[[2-(acetylamino)-  
3-methoxy-1,1-dimethyl-3-oxopropyl]dithio]ethyl]butylamino]carbonyl]oxy]-8-  
(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-  
benzofuranyl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



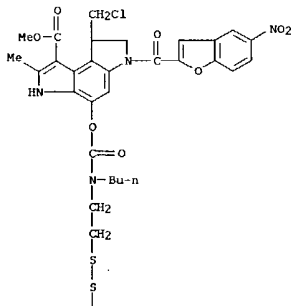
10/069,202

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



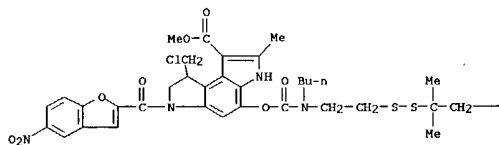
RN 477209-92-0 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-(2-pyridinyldithio)ethyl]amino]carbonyloxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

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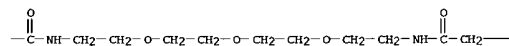


L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

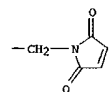
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RN 477209-95-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[31-8-(chloromethyl)-4-[[[31-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-2,7,7-trimethyl-1,9,29-trioxo-13,16,19,22,25-pentaosa-5,6-dithia-2,10,28-triazahentriacont-1-yl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

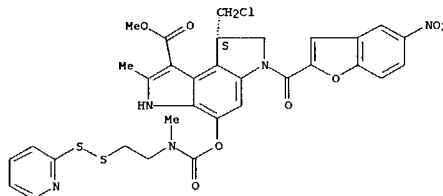
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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RN 477209-93-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-(2-pyridinyldithio)ethyl]amino]carbonyloxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester (85)- (9CI) (CA INDEX NAME)

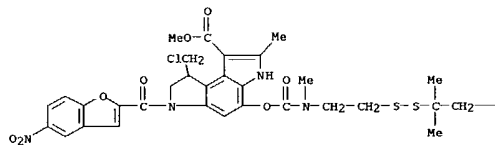
Absolute stereochemistry.



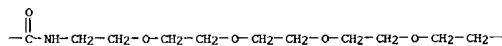
RN 477209-94-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-butyl-25-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-7,7-dimethyl-1,9,23-trioxo-13,16,19-trioxo-5,6-dithia-2,10,22-triazapentacos-1-yl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

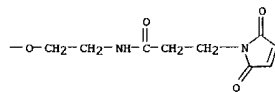
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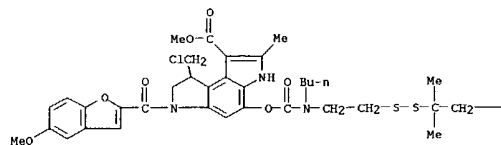


RN 477209-96-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-butyl-25-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-7,7-dimethyl-1,9,23-trioxo-13,16,19-trioxo-5,6-dithia-2,10,22-triazapentacos-1-yl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

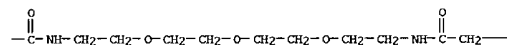
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L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

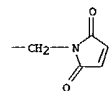
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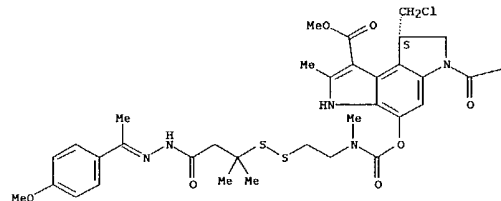


RN 477209-97-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-

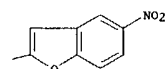
tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-4-[(2,7,7,14-pentamethyl-1,9,12-trioxo-13-oxa-5,6-dithia-2,10,11-triazapentadec-1-yl)oxy]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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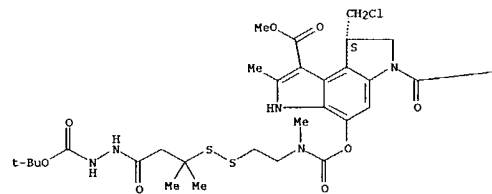


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8-(chloromethyl)-4-[[[2-  
[[[1,1-dimethyl-3-oxo-3-[[[1-(4-(3,6,9,12-tetraoxatridec-1-  
yloxy)phenyl]ethylidene]hydrazino]propyl]dithio]ethyl]methylamino]carbonyl  
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methyl ester, (8S)- (9CI) (CA INDEX NAME)

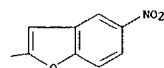
Absolute stereochemistry.  
Double bond geometry unknown.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
Absolute stereochemistry.

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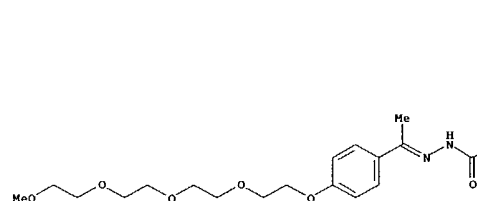


RN 477209-98-6 CAPLUS  
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8-(chloromethyl)-3,6,7,8-  
tetrahydro-4-[[[2-[[[1-(4-methoxyphenyl)ethylidene]hydrazino]-1,1-  
dimethyl-3-oxopropyl]dithio]ethyl]methylamino]carbonyl]oxy]-2-methyl-6-[(5-  
nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX  
NAME)

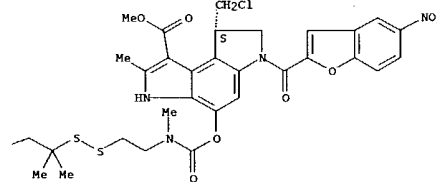
Absolute stereochemistry.  
Double bond geometry unknown.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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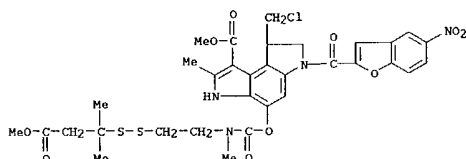
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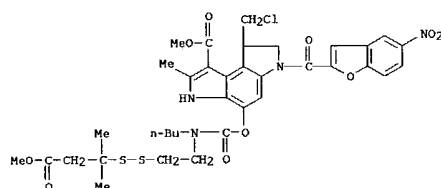
RN 477210-00-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-4-[[[2-[[[3-methoxy-1,1-dimethyl-3-  
oxopropyl]dithio]ethyl]methylamino]carbonyl]oxy]-2-methyl-6-[(5-nitro-2-  
benzofuranyl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

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L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477210-01-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 4-[[[butyl[2-[(3-methoxy-1,1-dimethyl-3-oxopropyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-methyl ester (9CI) (CA INDEX NAME)

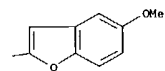


RN 477210-02-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-methoxy-2-benzofuranyl)carbonyl]-4-[[[methyl[2-(2-pyridinyl)dithio]ethyl]amino]carbonyl]oxy]-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

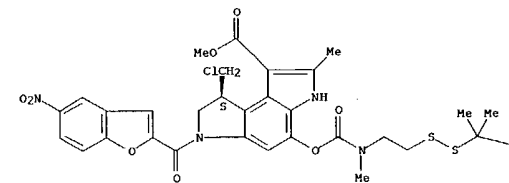
PAGE 1-B



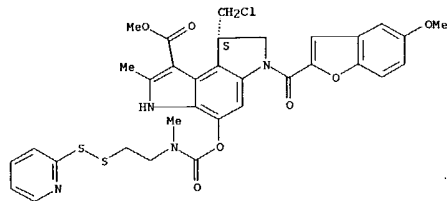
RN 477210-04-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-4-[[[2-[[[3-[[[1-[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)phenyl]ethylidene]hydrazino]-1,1-dimethyl-3-oxopropyl]dithio]ethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.

PAGE 1-A



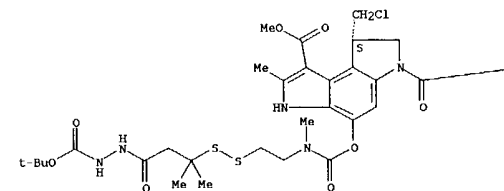
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477210-03-0 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-4-[(2,7,7,14,14-pentamethyl-1,9,12-trioxo-13-oxa-5,6-dithia-2,10,11-triazapentadec-1-yl)oxy]-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

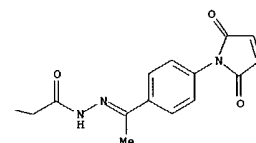
Absolute stereochemistry.

PAGE 1-A



L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

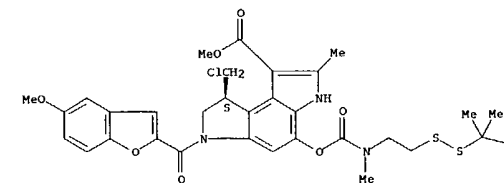
PAGE 1-B



RN 477210-05-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-4-[[[2-[[[3-[[[1-[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)phenyl]ethylidene]hydrazino]-1,1-dimethyl-3-oxopropyl]dithio]ethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.

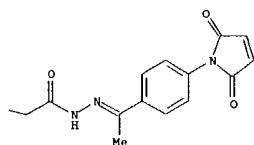
PAGE 1-A



10/069,202

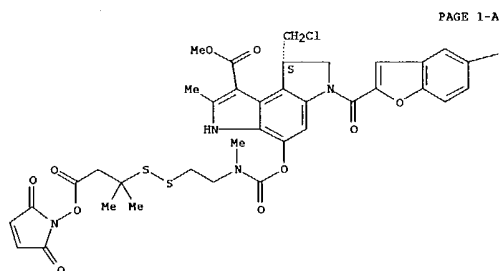
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B



RN 477210-06-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-4-[[[2-  
 [(3-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)oxy]-1,1-dimethyl-3-oxopropyl)dithio]ethyl]methylamino]carbonyl]oxy]-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

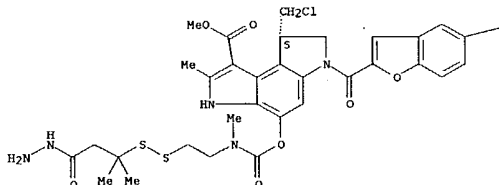
Absolute stereochemistry.



PAGE 1-A

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

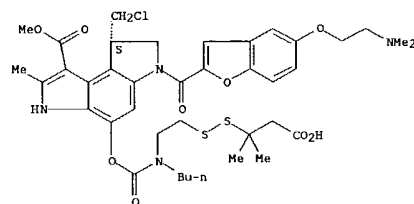


PAGE 1-B

OMe

RN 477210-09-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 4-[[[butyl[2-[(2-carboxy-1,1-dimethylethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477210-10-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 4-[(2-butyl-7,7,14,14-tetramethyl-1,9,12-trioxo-13-oxa-5,6-dithia-2,10,11-triazapentadec-1-yl)oxy]-8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)-

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

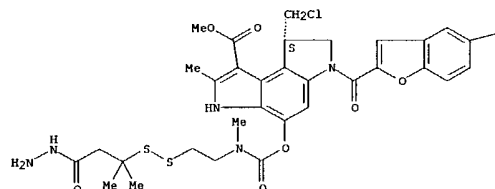
PAGE 1-B



RN 477210-07-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-4-[[[2-  
 [(3-hydrazino-1,1-dimethyl-3-oxopropyl)dithio]ethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[5-nitro-2-benzofuranyl]carbonyl]-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

NO2

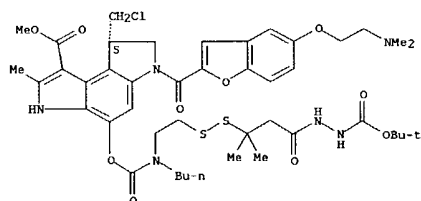
RN 477210-08-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-4-[[[2-  
 [(3-hydrazino-1,1-dimethyl-3-oxopropyl)dithio]ethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[[5-methoxy-2-benzofuranyl]carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

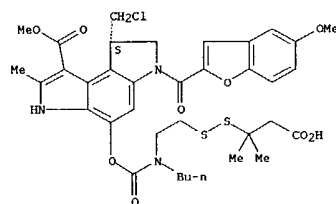
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477210-11-0 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 4-[[[butyl[2-[(2-carboxy-1,1-dimethylethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[5-methoxy-2-benzofuranyl]carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



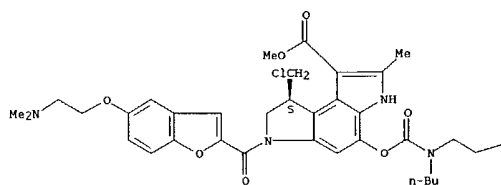
RN 477210-12-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 4-[[[butyl[2-[[3-[[1,4-4-  
 [(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutoxy]phenyl]ethylidene]hydrazino]-1,1-dimethyl-3-oxopropyl]dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

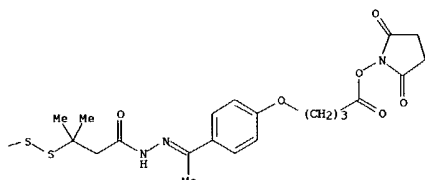
10/069,202

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
Double bond geometry unknown.

PAGE 1-A



PAGE 1-B

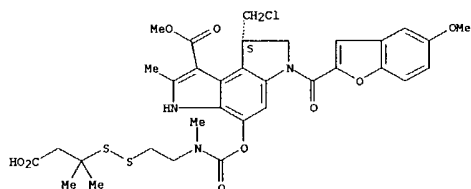


RN 477210-13-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,1-dimethyl-3-oxopropyl]dithio]ethyl]amino]carbonyloxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

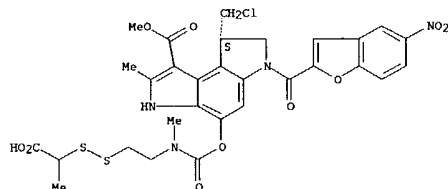
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.



RN 477210-16-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[(1-carboxyethyl)dithio]ethyl]methylamino]carbonyloxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-nitro-2-benzofuranyl)carbonyl]-1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

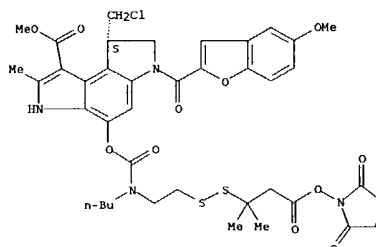
Absolute stereochemistry.



RN 477210-17-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[(2-carboxy-1,1-dimethylethyl)dithio]ethyl]amino]carbonyloxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

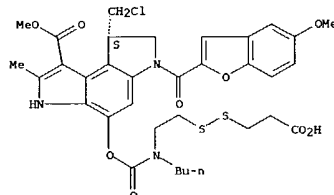
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



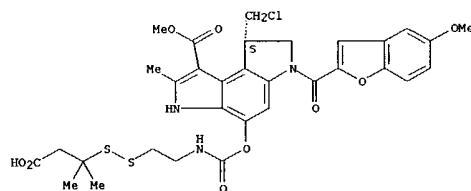
RN 477210-14-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(2-carboxyethyl)dithio]ethyl]amino]carbonyloxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



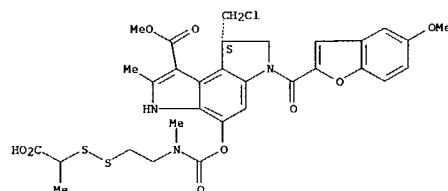
RN 477210-15-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[(2-carboxy-1,1-dimethylethyl)dithio]ethyl]methylamino]carbonyloxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477210-18-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[(1-carboxyethyl)dithio]ethyl]methylamino]carbonyloxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

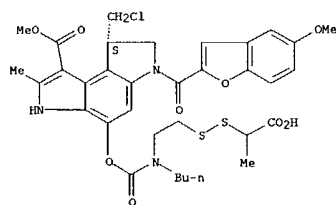


RN 477210-19-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(1-carboxyethyl)dithio]ethyl]amino]carbonyloxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

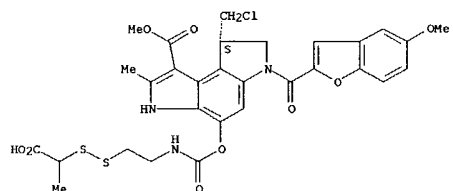
10/069,202

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477210-20-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[(1-methylethyl)dithio]ethyl]amino]carbonyloxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

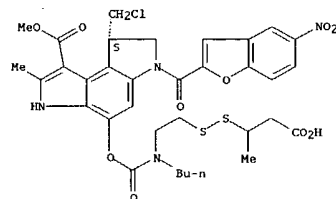
Absolute stereochemistry.



RN 477210-21-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(1-methylethyl)dithio]ethyl]amino]carbonyloxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

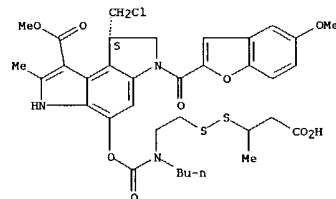
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477210-24-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[(2-carboxy-1-methylethyl)dithio]ethyl]amino]carbonyloxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

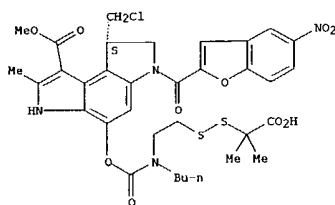
Absolute stereochemistry.



RN 477210-25-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[(2-carboxy-1-methylethyl)dithio]ethyl]amino]carbonyloxy]-8-(chloromethyl)-6-[[[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

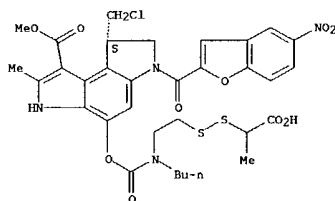
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477210-22-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(1-methylethyl)dithio]ethyl]amino]carbonyloxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

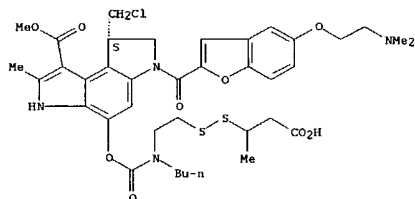
Absolute stereochemistry.



RN 477210-23-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(2-carboxy-1-methylethyl)dithio]ethyl]amino]carbonyloxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

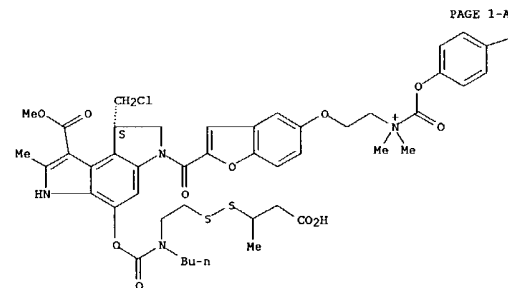
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477210-26-7 CAPLUS  
CN Ethanaminium, 2-[[[2-[[[1S]-5-[[[butyl[2-[(2-carboxy-1-methylethyl)dithio]ethyl]amino]carbonyloxy]-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]oxy]-N,N-dimethyl-N-[(4-nitrophenoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



NO2

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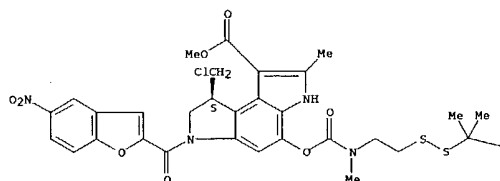
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L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

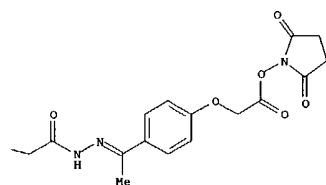
RN 477210-27-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-4-[[[2-  
 [[3-[[1-[4-[2-(2,5-dioxo-1-pyrrolidinyl)oxy]-2-  
 oxoethoxy]phenyl]ethylidene]hydrazino]-1,1-dimethyl-3-  
 oxopropyl]dithio]ethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-  
 methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.

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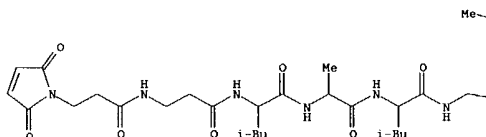
RN 477328-57-7 CAPLUS  
 CN Leucinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

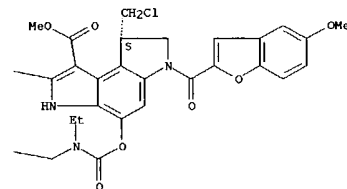
tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-1-(methoxycarbonyl)-2-  
 methylbenzo[1,2-b:4,3-b']dipyrrole-4-yl]oxy]carbonyl]ethylamino]ethyl]-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



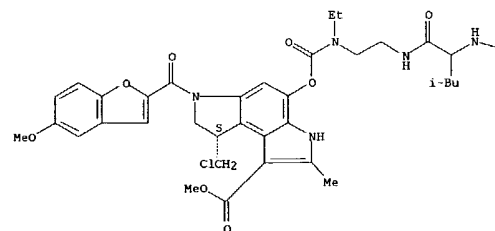
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

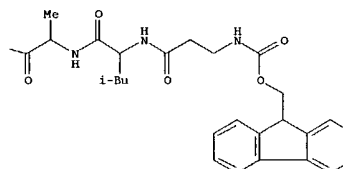
alanylleucylalanyl-N-[2-[[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-  
 methoxy-2-benzofuranyl)carbonyl]-1-(methoxycarbonyl)-2-methylbenzo[1,2-  
 b:4,3-b']dipyrrole-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.

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RN 477328-58-8 CAPLUS  
 CN Leucinamide, N-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-  
 β-alanylleucylalanyl-N-[2-[[[[(8S)-8-(chloromethyl)-3,6,7,8-

L14 ANSWER 6 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:755199 CAPLUS  
 DN 137:284323  
 TI Enzyme-cleavable prodrug compounds  
 IN Dubois, Vincent; Fernandez, Anne Marie; Gangwar, Sanjeev; Lewis, Evan;  
 Lobl, Thomas J.; Nieder, Matthew H.; Pickford, Lesley B.; Trouet,  
 Andre;  
 Yarranton, Geoffrey T.  
 PA Belg.  
 SO U.S. Pat. Appl. Publ., 86 pp., Cont.-in-part of Appl. No.  
 PCT/US99/30393.  
 CODEN: USXXCO  
 DT Patent  
 LA English  
 FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2002142955	A1	20021003	US 2001-879442	20010611
WO 2000033888	A2	20000615	WO 1999-US30393	19991210
WO 2000033888	A3	20011108		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,  
 CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID,  
 IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,  
 MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,  
 SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,  
 AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,  
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 PRAI US 1998-111793P P 19981211  
 US 1999-119312P P 19990208  
 WO 1999-US30393 A2 19991210  
 US 2000-211887P P 20000614  
 US 2001-290448P P 20010511

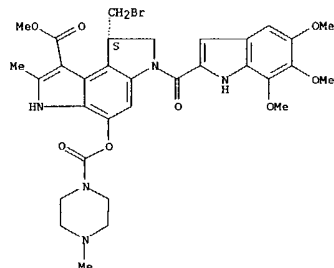
OS MARPAT 137:284323  
 AB The prodrug of the invention is a modified form of a therapeutic  
 agent and  
 comprises a therapeutic agent, an oligopeptide, a stabilizing group  
 and,  
 optionally, a linker group. The prodrug is cleavable by the enzyme  
 Thimet  
 oligopeptidase, or TOP. Also disclosed are methods of designing  
 prodrugs  
 by utilizing TOP-cleavable sequences within the conjugate and methods  
 of  
 treating patients with prodrugs of the invention.  
 IT 154889-68-6, Kw-2189  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (thimet oligopeptidase-cleavable prodrug compds.)  
 RN 154889-68-6 CAPLUS

10/069,202

L14 ANSWER 6 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



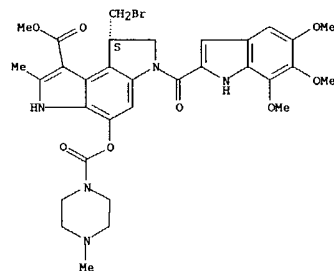
L14 ANSWER 7 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 occupied by B16-B16 colonies to the non-affected one to 8.2±1.8% (P<0.01), compared to 45.7±12.6% and 44.0±6.3% for non-treated and doxorubicin (5.2 µmol/kg)-treated animals. The same prodrug at 69.0 µmol/kg provided 1.5±0.6% of surface affected.

IT 154889-68-6, KW-2189  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (oligopeptide-based prodrugs activated by plasmin for chemotherapy)

RN 154889-68-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:157495 CAPLUS

DN 136:205412

TI Oligopeptide-based prodrugs activated by plasmin and their use in cancer chemotherapy

IN Trouet, Andre; Dubois, Vincent; Passioudou, Alexandre

PA Coulter Pharmaceutical, Inc., USA

SO PCT Int. Appl., 67 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002015700	A1	20020228	WO 2001-US26476	20010823
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001086727	A5	20020304	AU 2001-86727	20010823
PRAI US 2000-227686P	P	20000824		
WO 2001-US26476	W	20010823		
OS MARPAT 136:205412				

AB A prodrug, cleavable by plasmin, comprises a therapeutic agent capable of entering a target cell, e.g., a tumor or inflammatory cell, an oligopeptide having a plasmin peptide substrate of 2-4 amino acids and mono- or di-peptide linkage, a stabilizing group and, optionally, a linker group. Also disclosed are methods of making and using the prodrug compds.

For example, the activity of D-Ala-Leu-Lys-Leu-Leu-doxorubicin (I) (preparation given) was evaluated in the B16-B16 murine melanoma model. The mice receiving the prodrug did not show any important weight loss during the experiment and no clin. signs of toxicity were observed. At the same time, the drug had a marked effect on the metastatic growth. At 34.5 µmol/kg, I reduced the spread of lung metastases with a decrease of the ratio of the surface

L14 ANSWER 8 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:10314 CAPLUS

DN 136:86054

TI Tripeptide prodrug compounds

IN Bebbington, Christopher R.; Dubois, Vincent; Gangwar, Sanjeev; Lobl, Thomas J.; Nieder, Matthew H.; Pickford, Leslie B.; Trouet, Andre; Yarranton, Geoffrey T.

PA Corixa Corporation, USA

SO PCT Int. Appl., 102 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000263	A2	20020103	WO 2001-US40925	20010611
WO 2002000263	A3	20020815		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1294403	A2	20030326	EP 2001-942249	20010611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004501875	T2	20040122	JP 2002-505044	20010611
US 2003181359	A1	20030925	US 2002-311519	20021213
PRAI US 2000-212880P	P	20000614		
WO 2001-US40925	W	20010611		
OS CASREACT 136:86054; MARPAT 136:86054				

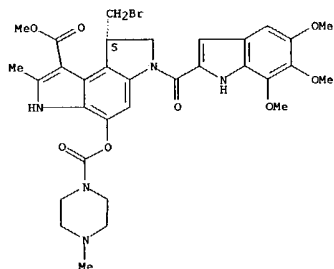
AB The prodrug of the invention is a modified form of a therapeutic agent and comprises a therapeutic agent, an oligopeptide AA3-AA2-AA1 (AA1 is leucine, phenylalanine, isoleucine, alanine, glycine, tyrosine, 2-naphthylalanine, or serine; AA2 is alanine, leucine, tyrosine, glycine, serine, 3-pyridylalanine, 2-thienylalanine, aminoisobutyric acid, threonine, or phenylalanine; AA3 is leucine, sarcosine, tyrosine, phenylalanine, p-chloro- or p-nitrophenylalanine, valine, norleucine, norvaline, phenylglycine, tryptophan, tetrahydroisoquinoline-3-carboxylic acid, 3-pyridylalanine, alanine, glycine, 2-thienylalanine, methionine, or proline), a stabilizing group and, optionally, a linker group. The prodrug is cleavable by a trouase enzyme such as Thimet oligopeptidase.



10/069,202

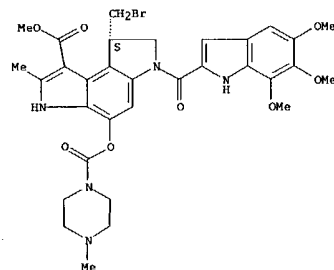
L14 ANSWER 8 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 Thus, Suc-Leu-Ala-Leu-Dox (Suc = succinic acid residue, Dox = doxorubicin residue), prepd. by conjugation of doxorubicin hydrochloride with Fmoc-Leu-Ala-Leu-OH, deprotection, and acylation with succinic anhydride, showed tumor-activated prodrug activity on LNCaP, HT-29 and PC-3 cells of 0.016, 0.052, and 0.075  $\mu$ M, resp. Suc-Leu-Ala-Leu-Dox is better tolerated in vivo than is doxorubicin.  
 IT 154889-68-6, KW 2189  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (tripeptide prodrug compds.)  
 RN 154889-68-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 9 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 RN 154889-68-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 9 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2001:923644 CAPLUS  
 DN 136:74618  
 TI Enzyme-cleavable prodrug compounds  
 IN Nieder, Matthew H.; Dubois, Vincent; Gangwar, Sanjeev; Lobl, Thomas J.; Pickford, Leslie B.; Trouet, Andre; Yarranton, Geoffrey T.  
 PA Corixa Corporation, USA  
 SO PCT Int. Appl., 159 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001095945	A2	20011220	WO 2001-US18903	20010611
WO 2001095945	A3	20020815		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 EP 1294405 A2 20030326 EP 2001-950291 20010611  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
 JP 2004510703 T2 20040408 JP 2002-510122 20010611  
 PRAI US 2000-211887P P 20000614  
 US 2001-290448P P 20010511  
 WO 2001-US18903 W 20010611  
 OS MARPAT 136:58787  
 AB The prodrug of the invention is a modified form of a therapeutic agent and comprises a therapeutic agent, an oligopeptide, a stabilizing group and, optionally, a linker group. The prodrug is cleavable by the enzyme, thimet oligopeptidase (TOP). Also disclosed are methods of designing prodrugs by utilizing TOP-cleavage sequences within the conjugate and methods of treating patients with prodrugs of the invention.  
 IT 154889-68-6, KW-2189  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (enzyme-cleavable prodrug compds.)

L14 ANSWER 10 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2001:923642 CAPLUS  
 DN 136:74618  
 TI Prodrug compounds with isoleucine  
 IN Pickford, Leslie B.; Gangwar, Sanjeev; Lobl, Thomas J.; Nieder, Matthew H.; Yarranton, Geoffrey T.  
 PA Corixa Corporation, USA  
 SO PCT Int. Appl., 107 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001095943	A2	20011220	WO 2001-US18857	20010611
WO 2001095943	A3	20020829		

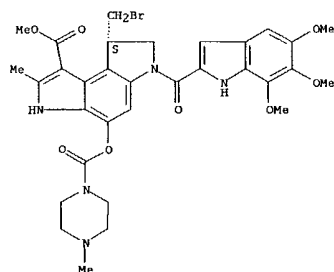
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 EP 1294404 A2 20030326 EP 2001-944442 20010611  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
 JP 2004510702 T2 20040408 JP 2002-510120 20010611  
 US 2004039160 A1 20040226 US 2002-311411 20021213  
 PRAI US 2000-211686P P 20000614  
 WO 2001-US18857 W 20010611  
 OS MARPAT 136:74618  
 AB The compds. of the invention are modified forms of therapeutic agents. A typical prodrug compound of the invention comprises a therapeutic agent, an oligopeptide having an isoleucine residue, a stabilizing group and, optionally, a linker group. The prodrug is cleavable by an enzyme associated with the target cell. Methods of making and using the compds. are also disclosed.  
 IT 154889-68-6, KW-2189  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (prodrug compds. with isoleucine)  
 RN 154889-68-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

10/069,202

L14 ANSWER 10 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-[[[5,6,7-trimethoxy-1H-indol-2-yl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 11 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:479762 CAPLUS

DN 135:81987

TI Sterilization of hardly water-soluble compounds by filtration

IN Kato, Hiromi; Tashiro, Yoshikazu

PA Kyowa Hakko Kogyo Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 5 pp.

CODEN: JKKXAF

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001181207	A2	20010703	JP 1999-369550	19991227
JP 1999-369550		19991227		

OS MARPAT 135:81987

AB Hardly water-soluble pharmaceutically active agents, especially antitumor DC-89

deriva., are entrapped in liposomes having an average particle size of  $\leq 0.2 \mu\text{m}$  and an injectable solution containing the liposomes is sterilizable by filtration.

IT 347174-93-0

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (sterilization of hardly water-soluble compds. entrapped in liposomes by

filtration)

RN 347174-93-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,

8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[4-methyl-1-piperazinyl]methyl]benzoyl]oxy]-, methyl ester, (8S)- (9CI)

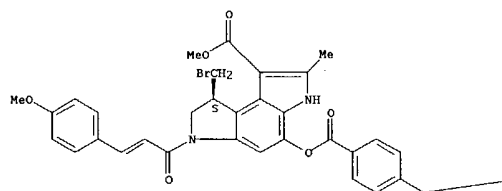
(CA INDEX NAME)

Absolute stereochemistry.

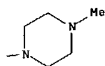
Double bond geometry unknown.

L14 ANSWER 11 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



L14 ANSWER 12 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:315940 CAPLUS

DN 135:76706

TI Derivatives of Methyl 5-Methyl-4-oxo-1,2,4,5,8,8a-hexahydrocyclopropa[c]-pyrrolo[3,2-e]indole-7-carboxylate: A Case of Inverse Electronic

Effects on the Reactivity of CC-1065 Derivatives

AU Castedo, Luis; Delamano, Jose; Enjo, Juan; Fernandez, Jesus; Gravalos, Dolores G.; Leis, Ramon; Lopez, Carmen; Marcos, Carlos F.; Rios, Ana; Tojo, Gabriel

CS Departamento de Quimica Organica, Unidad Asociada al CSIC Universidad

de

Santiago de Compostela, Santiago de Compostela, 15706, Spain

SO Journal of the American Chemical Society (2001), 123(21), 5102-5103

CODEN: JACSAT; ISSN: 0002-7863

American Chemical Society

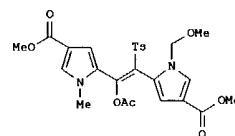
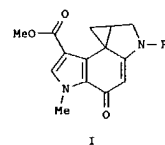
Journal

DT English

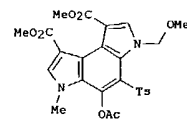
LA English

OS CASREACT 135:76706

GI



II



III

AB A series of Me 5-methyl-4-oxo-1,2,4,5,8,8a-hexahydrocyclopropa[c]-pyrrolo[3,2-e]indole-7-carboxylate derivs., I (R = H, CONH2, CO2C(Me)3, COMe, or SO2ME), were prepared. A key reaction was the photochem. oxidative

10/069,202

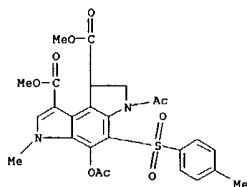
L14 ANSWER 12 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
cyclization of bis-pyrrolethene II to produce intermediate III.

These novel 5-methyl-cyclopropaindolones were found to exhibit a non-linear solvolytic behavior, with a region of increased reactivity (log k) correlating with decreased electron-deficiency as reflected by the  $\rho$  Hammett const. of their R substituents. Cyclopropaindolones I (R = H, CONH<sub>2</sub>, CO<sub>2</sub>C(Me)<sub>3</sub>, COMe, or SO<sub>2</sub>Me) also show an abnormal relationship between solvolytic reactivity and in vitro cytotoxic potency relative to other CC-1065 analogs, with those compds. with greater potency also having greater solvolytic reactivity.

IT 170431-00-2P 170431-01-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT (Reactant or reagent)  
(Inverse electronic effects on the reactivity of 5-methyl-cyclopropaindolone CC-1065 derivs)

RN 170431-00-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1,8-dicarboxylic acid,  
3-acetyl-5-(acetyloxy)-  
1,2,3,6-tetrahydro-6-methyl-4-[(4-methylphenyl)sulfonyl]-, dimethyl  
ester  
(9CI) (CA INDEX NAME)



RN 170431-01-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1,8-dicarboxylic acid,  
3-acetyl-5-(acetyloxy)-  
1,2,3,6-tetrahydro-6-methyl-4-[(4-methylphenyl)sulfonyl]-, dimethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 13 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2000:488720 CAPLUS  
DN 133:26627  
TI Synthesis and antitumor activity of duocarmycin derivatives: A-ring pyrrole compounds bearing  $\beta$ -(5',6',7'-trimethoxy-2'-indolyl)acryloyl group

AU Amishiro, N.; Nagamura, S.; Kobayashi, E.; Okamoto, A.; Gomi, K.; Okabe, M.; Saito, H.

CS Pharmaceutical Research Institute, Kyowa Hakko Kogyo Company, Ltd., Shizuoka, 411-8731, Japan

SO Bioorganic & Medicinal Chemistry (2000), 8(7), 1637-1643  
CODEN: BMECEP; ISSN: 0968-0896

PB Elsevier Science Ltd.

DT Journal

LA English

AB A series of A-ring pyrrole deriva. of duocarmycin bearing the  $\beta$ -(5',6',7'-trimethoxy-2'-indolyl)acryloyl group were synthesized, and evaluated for in vitro anticellular activity against HeLa S3 cells and in vivo antitumor activity against murine sarcoma 180 in mice. New

Seg-B analogs bearing the  $\beta$ -(5',6',7'-trimethoxy-2'-indolyl)acryloyl group containing a double bond as a spacer had lower peripheral blood toxicity than the derivs. bearing the 5',6',7'-trimethoxyindole-2'-carboxyl group

in Seg-B of the natural type. Moreover, most of them exhibited potent antitumor activity against in vivo murine tumor models.

IT 154889-68-6  
RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); BIOL (Biological study)

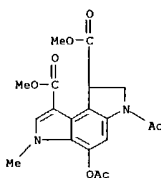
(preparation and antitumor activity of duocarmycin derivs.)

RN 154889-68-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

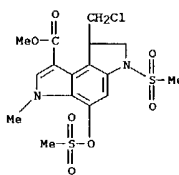
Absolute stereochemistry.

L14 ANSWER 12 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



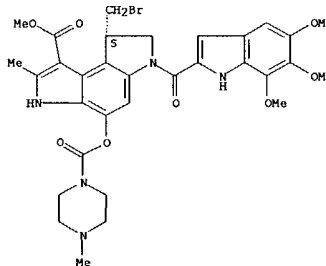
IT 346669-65-6P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(Inverse electronic effects on the reactivity of 5-methyl-cyclopropaindolone CC-1065 derivs)

RN 346669-65-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-3-methyl-6-(methylsulfonyl)-4-[(methylsulfonyl)oxy]-,  
methyl ester (9CI) (CA INDEX NAME)



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 13 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 297137-23-6P  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation);

BIOL (Biological study); PREP (Preparation)  
(preparation and antitumor activity of duocarmycin derivs.)

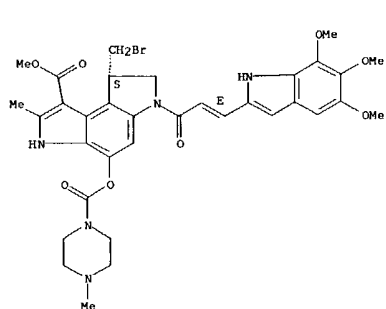
RN 297137-23-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)-1-oxo-2-propenyl]-, methyl ester, monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

10/069,202

L14 ANSWER 13 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



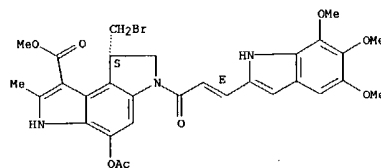
PAGE 2-A

● HBr

IT 297137-24-7P 297137-25-8P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (preparation and antitumor activity of duocarmycin derivs.)  
 RN 297137-24-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(2E)-3-(5,6,7-trimethoxy-1H-indol-2-yl)-1-oxo-2-propenyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.

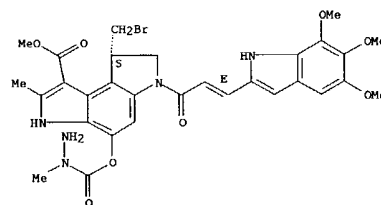
L14 ANSWER 13 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 297137-25-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[(1-methylhydrazino)carbonyloxy]-6-[(2E)-3-(5,6,7-trimethoxy-1H-indol-2-yl)-1-oxo-2-propenyl]-, methyl ester, (8S)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.

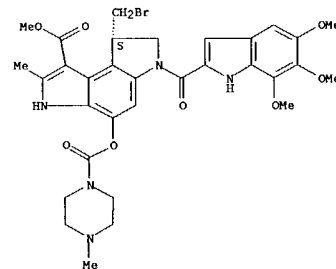


RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 14 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2000:424475 CAPLUS  
 DN 133:26526  
 TI A phase II pilot study of KW-2189 in patients with advanced renal cell carcinoma  
 AU Small, Eric J.; Figlin, Robert; Petrylak, Daniel; Vaughn, David J.; Sartor, Oliver; Horak, Ivan; Pincus, Rosemarie; Kramer, Alton; Bowden, Chris  
 CS UCSF Comprehensive Cancer Center, University of California, San Francisco, CA, USA  
 SO Investigational New Drugs (2000), 18(2), 193-197  
 CODEN: INNDUK; ISSN: 0167-6997  
 PB Kluwer Academic Publishers  
 DT Journal  
 LA English  
 AB KW-2189 is a semi-synthetic, water-soluble analog of duocarmycin B2, a new class of potent antitumor antibiotics produced by streptomyces, with improved in vitro antitumor potency. Forty patients with pathol. confirmed metastatic renal cell carcinoma were treated in this multicenter, open-label phase II trial. All patients received 0.4 mg/m<sup>2</sup> KW-2189 as an IV infusion for Cycle 1. Cycles were repeated every 5 to 6 wk with escalations to 0.5 mg/m<sup>2</sup> in the absence of significant toxicity or disease progression. No patient had an objective response. The most common drug-related toxicity was hematol.-delayed neutropenia and thrombocytopenia, with recovery by week 6. Non-hematol. toxicity consisted of mild to moderate fatigue, nausea and vomiting, and anorexia that was generally manageable. KW-2189 in this dose and schedule has a predictable safety profile of reversible myelosuppression. No activity in metastatic renal cell carcinoma was demonstrated.  
 IT 154889-68-5, KW-2189  
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (phase II pilot study of KW-2189 in patients with advanced renal cell carcinoma)  
 RN 154889-68-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[(4-methyl-1-piperazinyl)carbonyloxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 14 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



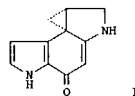
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/069,202

L14 ANSWER 15 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AN 2000:401690 CAPLUS  
 DN 133:48878  
 TI Oligopeptide prodrug compounds and process for preparation thereof  
 IN Lohi, Thomas J.; Dubois, Vincent; Fernandez, Anne-Marie; Gangwar, Sanjeev; Lewis, Evan; Nieder, Matthew H.; Trouet, Andre; Viski, Peter; Yarranton, Geoffrey T.  
 PA Coulter Pharmaceutical, Inc., USA  
 SO PCT Int. Appl., 125 pp.  
 CODEN: PXXXX2  
 DT Patent  
 LA English  
 FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000033888	A2	20000615	WO 1999-US30393	19991210
WO 2000033888	A3	20011108		

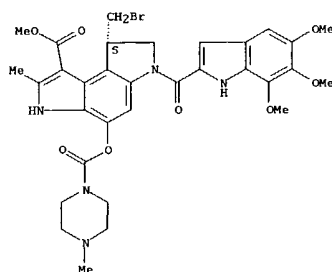
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 EP 1144011 A2 20011017 EP 1999-967462 19991210  
 EP 1144011 A3 20020206  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO  
 JP 2003518000 T2 20030603 JP 2000-586378 19991210  
 AU 773420 B2 20040527 AU 2000-23733 19991210  
 US 2002142955 A1 20021003 US 2001-879442 20010611  
 PRAI US 1998-111793P P 19981211  
 US 1999-119312P P 19990208  
 WO 1999-US30393 W 19991210  
 US 2000-211887P P 20000614  
 US 2001-290448P P 20010511  
 OS MARPAT 133:48878  
 AB The prodrug of the invention is a modified form of a therapeutic agent and comprises a therapeutic agent, an oligopeptide, a stabilizing group and,



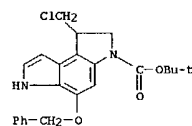
AB Synthesis of  
 1,2,8,8a-tetrahydrocyclopropa[c]pyrrolo[3,2-e]indol-4(5H)-one  
 (I), the parent CC-1065 and duocarmycin SA alkylation subunit, is detailed. The parent CFI alkylation subunit lacks the C7 Me substituent of the CC-1065 alkylation subunit and the C6 methoxycarbonyl group of duocarmycin SA, and their examination permitted the establishment of the impact of these natural product substituents. The studies revealed a CPI stability comparable to the CC-1065 alkylation subunit but which was 6x more reactive than the (+)-duocarmycin SA alkylation subunit, and it displayed the inherent reaction regioselectivity (4:1) of the natural products. The single-crystal X-ray structure of (+)-N-BOC-CFI depicts a near identical stereoelectronic alignment of the cyclopropane accounting for the identical reaction regioselectivity and a slightly diminished vinylogous amide conjugation relative to (+)-N-BOC-DSA suggesting that the stability distinctions stem in part from this difference in the vinylogous amide as well as alterations in the electronic nature of the fused pyrrole. Establishment of the DNA binding properties revealed that the

L14 ANSWER 15 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)  
 optionally, a linker group. The prodrug is cleavable by the enzyme trypsin. Also disclosed are processes for making the prodrug compds.  
 IT 154889-68-6, KW-2189  
 RI: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (oligopeptide prodrug compds. and process for preparation thereof)  
 RN 154889-68-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



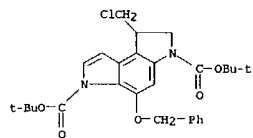
L14 ANSWER 16 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)  
 CPI-based agents retain the identical DNA alkylation selectivities of the natural products. More importantly, the C6 methoxycarbonyl group of duocarmycin SA was found to increase the rate (12-13x) and efficiency (10x) of DNA alkylation despite its intrinsic lower reactivity while the CC-1065 C7 Me group was found to slow the DNA alkylation rate (4x) and lower the alkylation efficiency (ca. 4x). The greater DNA alkylation rate and efficiency for duocarmycin SA and related analogs contg. the C6 methoxycarbonyl is proposed to be derived from the extended length that the rigid C6 methoxycarbonyl provides and the resulting increase in the DNA binding-induced conformational change which serves to deconjugate the vinylogous amide and activate the alkylation subunit for nucleophilic attack. The diminished properties resulting from the CC-1065 C7 Me group may be attributed to the steric impediment this substituent introduces to DNA minor groove binding and alkylation. Consistent with this behavior, the duocarmycin SA C6 methoxycarbonyl group increases biol. potency while the CC-1065 C7 Me group diminishes it.  
 IT 227084-68-6P 277317-35-8P  
 RI: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (synthesis and evaluation of tetrahydrocyclopropapyrroloindolones the parent alkylation subunit of CC-1065 and the duocarmycins)  
 RN 227084-68-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 277317-35-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3,6-dicarboxylic acid, 1-(chloromethyl)-1,2-dihydro-5-(phenylmethoxy)-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

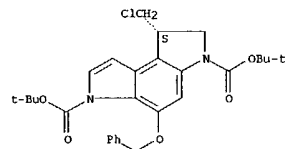
10/069,202

L14 ANSWER 16 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 277317-90-5P 277317-92-7P  
 RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)  
 (synthesis and evaluation of tetrahydrocyclopropapyrroloindolones the parent alkylation subunit of CC-1065 and the duocarmycins)  
 RN 277317-90-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrol-3,6-dicarboxylic acid, 1-(chloromethyl)-1,2-dihydro-5-(phenylmethoxy)-, bis(1,1-dimethylethyl) ester, (1S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



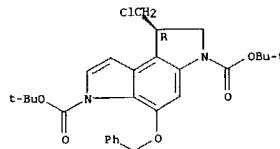
RN 277317-92-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrol-3,6-dicarboxylic acid, 1-(chloromethyl)-1,2-dihydro-5-(phenylmethoxy)-, bis(1,1-dimethylethyl) ester, (1R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:141730 CAPLUS  
 DN 132:334367  
 TI Synthesis and antitumor activity of duocarmycin derivatives: modification at C-8 position of A-ring pyrrole compounds bearing the simplified DNA-binding groups  
 AU Amishiro, N.; Nagamura, S.; Murakata, C.; Okamoto, A.; Kobayashi, E.; Asada, M.; Gomi, K.; Tamaoki, T.; Okabe, M.; Yamaguchi, N.; Yamaguchi, K.; Saito, H.  
 CS Pharmaceutical Research Institute, Kyowa Hakko Kogyo Company, Ltd., Nagazumi, Sunto, Shizuoka, Japan  
 SO Bioorganic & Medicinal Chemistry (2000), 8(2), 381-391  
 CODEN: BMECEP; ISSN: 0968-0896  
 PB Elsevier Science Ltd.  
 DT Journal  
 LA English  
 OS CASREACT 132:334367  
 AB A series of the 8-O-substituted A-ring pyrrole derivs. of duocarmycin bearing the simplified DNA-binding moieties such as cinnamoyl or heteroaryl-acryloyl groups were synthesized, and evaluated for in vitro anticellular activity against HeLa S3 cells and in vivo antitumor activity against murine sarcoma 180 in mice. In addition, the stability of the 8-O-substituted analogs in aqueous solution and the conversion to their active form (cyclopropane compound) from the 8-O-substituted analogs in mice or human serum were examined. The 8-O-substituted A-ring pyrrole derivs. bearing the simplified DNA-binding moieties showed remarkably potent in vivo antitumor activity and low peripheral blood toxicity compared with the 8-O-substituted A-ring pyrrole derivs. having the trimethoxyindole skeleton in segment-B (Seg-B), which were equal to 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of 4'-methoxycinnamates and 4'-methoxy-β-heteroarylacrylates. Moreover, among 8-O-substituted analogs, several compds. can be chemical or enzymically converted to their active form in human serum. This result indicated that new 8-O-substituted derivs. were different prodrugs from KW-2189 and 8-O-substituted analogs being the same type of prodrug as KW-2189.  
 IT 160819-28-3 186760-06-5  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (synthesis and antitumor activity of duocarmycin derivs. modified at C-8 position of A-ring pyrrole compds. bearing the simplified DNA-binding groups)  
 RN 160819-28-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

L14 ANSWER 16 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

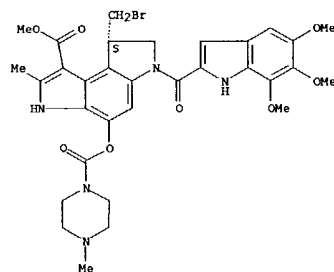


RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[[[5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-A

PAGE 2-A

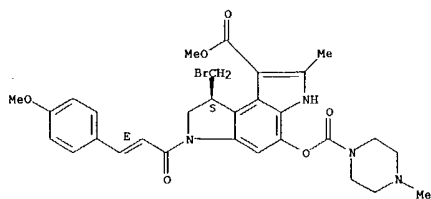
● HBr

RN 186760-06-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.

10/069,202

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



● HCl

IT 267899-52-5P

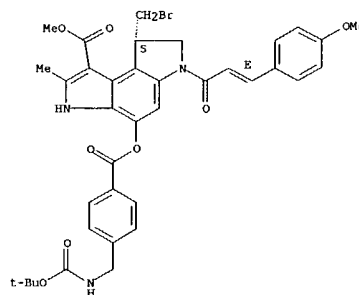
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent) (synthesis and antitumor activity of duocarmycin derivs. modified at C-8 position of A-ring pyrrole compds. bearing the simplified DNA-binding groups)

RN 267899-52-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(1,1-dimethylethoxy)carbonyl]amino]methyl]benzoyloxy]-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 267899-40-1P 267899-41-2P 267899-42-3P

267899-43-4P 267899-44-5P 267899-45-6P  
267899-46-7P 267899-47-8P 267899-48-9P  
267899-49-0P 267899-50-3P 267899-51-4P  
267899-53-6P 267899-54-7P 267899-55-8P  
267899-56-9P 267899-57-0P 267899-58-1P  
267899-59-2P 267899-60-5P 267899-61-6P  
267899-62-7P 267899-64-9P 267899-65-0P  
267899-66-1P 267899-67-2P 267899-68-3P  
267899-69-4P 267899-70-7P 267899-71-8P  
267899-72-9P 267899-73-0P

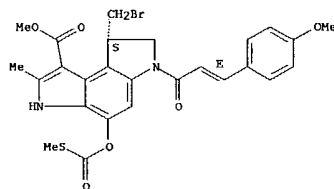
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (synthesis and antitumor activity of duocarmycin derivs. modified at C-8 position of A-ring pyrrole compds. bearing the simplified DNA-binding groups)

RN 267899-40-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(methylthio)carbonyloxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

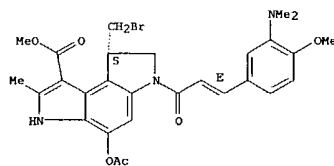
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 267899-41-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-6-[(2E)-3-{3-(dimethylamino)-4-methoxyphenyl}-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

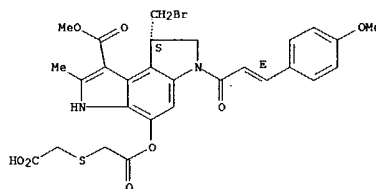


RN 267899-42-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(carboxymethyl)thio]acetyl]oxy]-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

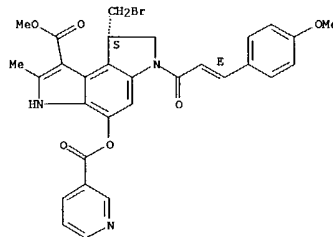
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 267899-43-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



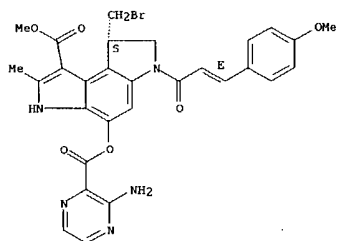
RN 267899-44-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[3-aminopyrazinyl]carbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

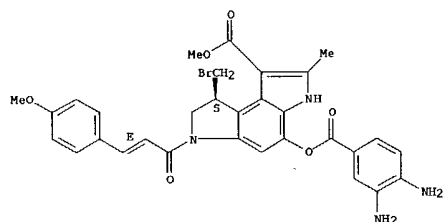
10/069,202

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 267899-45-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[(3,4-diaminobenzoyl)oxy]-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

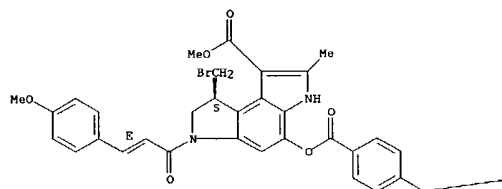


RN 267899-46-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
4-[(4-aminobenzoyl)oxy]-8-

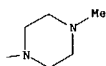
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

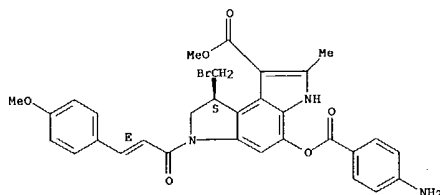


RN 267899-49-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

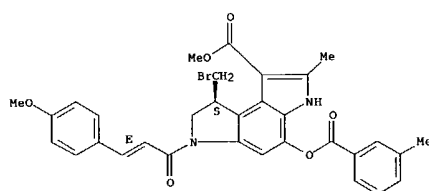
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



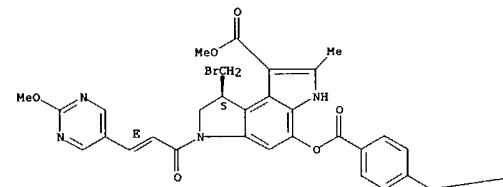
RN 267899-47-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(3-methylbenzoyl)oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

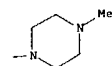


RN 267899-48-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
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PAGE 1-B



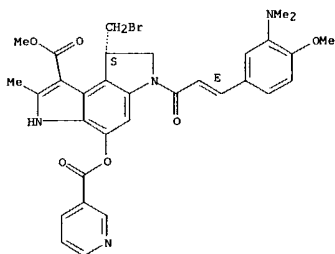
RN 267899-50-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-6-[(2E)-3-[(3-(dimethylamino)-4-methoxyphenyl)-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



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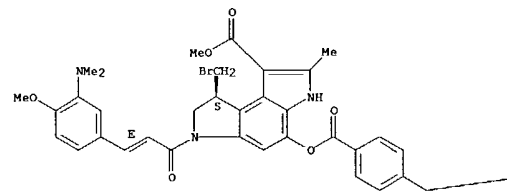
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 267899-51-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-6-[(2E)-3-  
[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-  
methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl  
ester, (8S)- (9CI) (CA INDEX NAME)

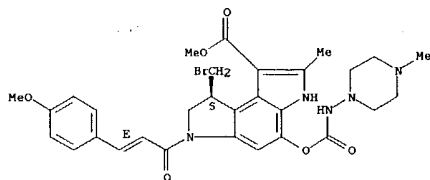
Absolute stereochemistry.  
Double bond geometry as shown.

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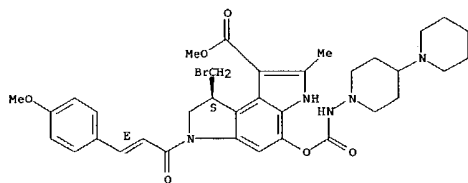
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



RN 267899-55-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
4-[[[(1,4'-bipiperidin)-1'-  
ylamino]carbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-  
methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

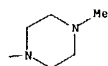


RN 267899-56-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(1-  
methylhydrazino)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX  
NAME)

Absolute stereochemistry.

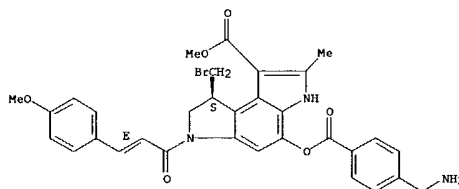
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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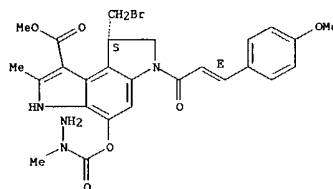
RN 267899-53-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[4-  
(aminomethyl)benzoyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-  
methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



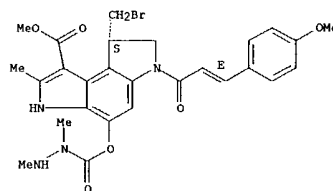
RN 267899-54-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-  
methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, (8S)- (9CI)  
(CA INDEX NAME)

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
Double bond geometry as shown.



RN 267899-57-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,2-  
dimethylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(2E)-3-(4-  
methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

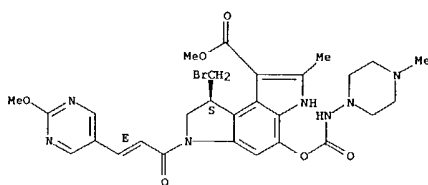


RN 267899-58-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-6-[(2E)-3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-  
4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, (8S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

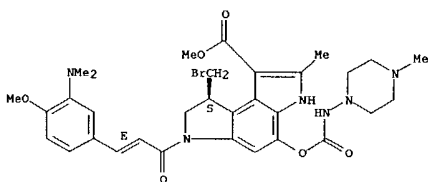
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L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)



RN 267899-59-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-6-[(2E)-3-  
[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-  
methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl  
ester, (8S)- (9CI) (CA INDEX NAME)

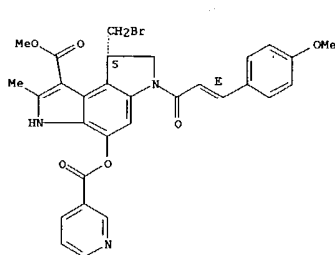
Absolute stereochemistry.  
Double bond geometry as shown.



RN 267899-60-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-6-[(2E)-3-  
[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-  
methyl-4-[[[(1-methylhydrazino)carbonyl]oxy]-, methyl ester, (8S)-  
(9CI) (CA INDEX NAME)

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)  
pyridinylcarbonyl]oxy]-, methyl ester, monohydrochloride, (8S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



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● HCl

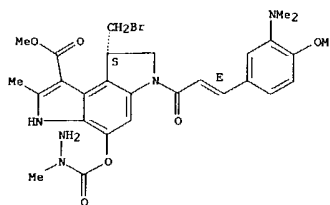
RN 267899-64-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-  
[[4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester,  
monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

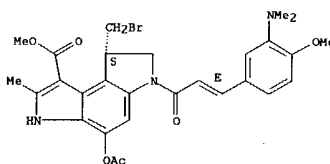
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)

Absolute stereochemistry.  
Double bond geometry as shown.



RN 267899-61-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-  
(bromomethyl)-6-[(2E)-3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-  
propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester,  
monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

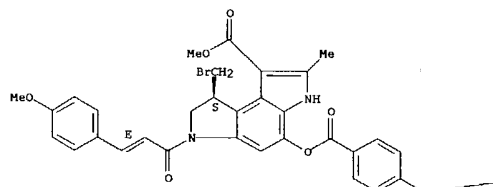


● HCl

RN 267899-62-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(3-

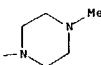
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)

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● HBr

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RN 267899-65-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

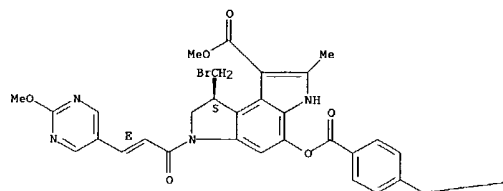
tetrahydro-6-[(2E)-3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-  
4-[[4-[[4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester,  
dihydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

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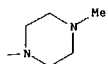
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



●2 HBr

PAGE 1-B



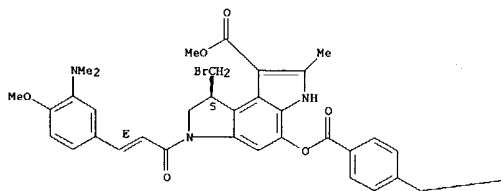
RN 267899-66-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[(2E)-3-

[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, dihydrobromide, (8S)- (9CI) (CA INDEX NAME)

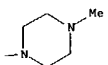
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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●2 HBr

PAGE 1-B



RN 267899-68-3 CAPLUS

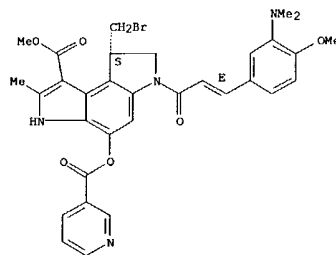
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[4-(aminomethyl)benzoyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.  
Double bond geometry as shown.

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●2 HBr

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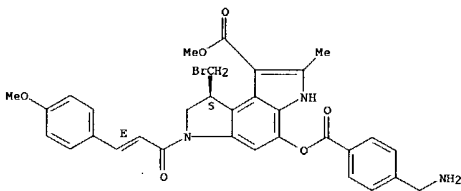
RN 267899-67-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[(2E)-3-

[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[4-(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester, dihydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

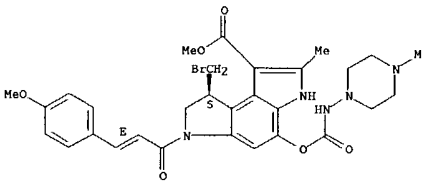


● HBr

RN 267899-69-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-methyl-1-piperazinyl]amino]carbonyl]oxy]-, methyl ester, dihydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

●2 HBr

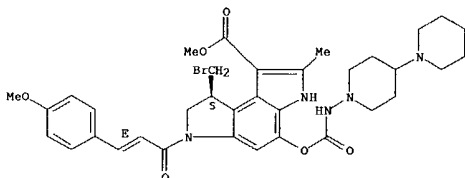
RN 267899-70-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[1,4'-bipiperidin]-1'-ylamino]carbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-

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L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester,  
dihydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



● 2 HBr

RN 267899-71-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

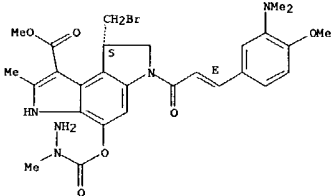
tetrahydro-6-[(2E)-3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-  
4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester,  
monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-6-[(2E)-3-

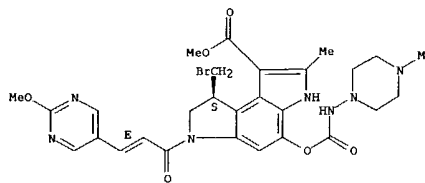
[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-  
methyl-4-[[[(1-methylhydrazino)carbonyl]oxy]-, methyl ester,  
dihydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



● 2 HBr

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

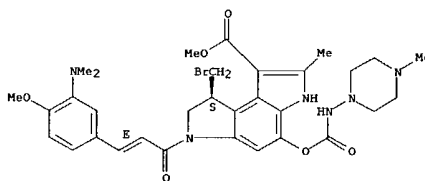


● HBr

RN 267899-72-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-6-[(2E)-3-

[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-  
methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl  
ester,  
monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

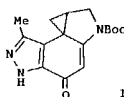
Absolute stereochemistry.  
Double bond geometry as shown.



● HBr

RN 267899-73-0 CAPLUS

L14 ANSWER 18 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1999:737584 CAPLUS  
DN 132:78392  
TI Resolution of a CP2I precursor, synthesis and biological evaluation  
of (+) and (-)-N-Boc-CP2I: a further validation of the relationship between  
chemical solvolytic stability and cytotoxicity  
AU Baraldi, Pier Giovanni; Cacciari, Barbara; Romagnoli, Romeo; Spalluto,  
Giampiero; Boyce, Christopher W.; Boger, Dale L.  
CS Dipartimento di Scienze Farmaceutiche, Università di Ferrara, Ferrara,  
44100, Italy  
SD Bioorganic & Medicinal Chemistry Letters (1999), 9(21), 3087-3092  
CODEN: BMCLER; ISSN: 0960-894X  
PB Elsevier Science Ltd.  
DT Journal  
LA English  
GI

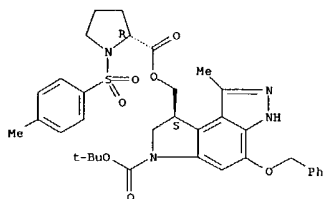


AB The chemical resolution, using N-tosyl-L-proline as a chiral  
auxiliary, of a  
racemate of the pyrazole analog (±)-N-Boc-CP2I (I) of the left hand  
segment (CPI) of the antitumor agent CC-1065, and the cytotoxic  
evaluation  
of both enantiomers are described. The reported results further  
validate  
the direct relationship between chemical solvolytic stability of the  
cyclopropane ring and cytotoxicity proposed by Boger and coworkers.  
IT 253598-42-4P 253598-46-8P  
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic  
preparation); PREP (Preparation); RACT (Reactant or reagent)  
(chemical resolution using N-tosyl-L-proline as a chiral auxiliary,  
solvolytic stability and cytotoxicity of CP2I moiety of CC-1065)  
RN 253598-42-4 CAPLUS  
CN D-Proline, 1-[(4-methylphenyl)sulfonyl]-, [(8S)-6-[(1,1-  
dimethylethoxy)carbonyl]-3,6,7,8-tetrahydro-1-methyl-4-  
(phenylmethoxy)pyrrolo[3,2-e]indazol-8-yl)methyl ester (9CI) (CA  
INDEX  
NAME)

Absolute stereochemistry. Rotation (-).

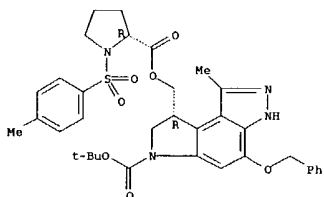
10/069,202

L14 ANSWER 18 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



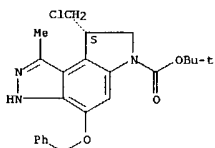
RN 253598-46-8 CAPLUS  
 CN D-Proline, 1-[(4-methylphenyl)sulfonyl]-, [(8R)-6-[(1,1-dimethylethoxy)carbonyl]-3,6,7,8-tetrahydro-1-methyl-4-(phenylmethoxy)pyrrolo[3,2-e]indazol-8-yl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



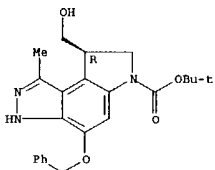
IT 187034-24-8  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (chemical resolution using N-tosyl-L-proline as a chiral auxiliary, solvolytic stability and cytotoxicity of CPZI moiety of CC-1065)  
 RN 187034-24-8 CAPLUS  
 CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-1-methyl-4-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 18 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



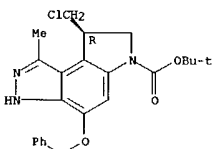
RN 253598-47-9 CAPLUS  
 CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-1-methyl-4-(phenylmethoxy)-, 1,1-dimethylethyl ester, (8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

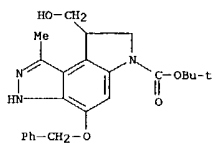


RN 253598-48-0 CAPLUS  
 CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 8-(chloromethyl)-7,8-dihydro-1-methyl-4-(phenylmethoxy)-, 1,1-dimethylethyl ester, (8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

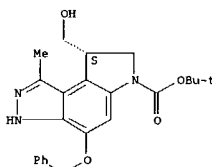


L14 ANSWER 18 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 253598-43-5P 253598-44-6P 253598-47-9P  
 253598-48-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (chemical resolution using N-tosyl-L-proline as a chiral auxiliary, solvolytic stability and cytotoxicity of CPZI moiety of CC-1065)  
 RN 253598-43-5 CAPLUS  
 CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-1-methyl-4-(phenylmethoxy)-, 1,1-dimethylethyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 253598-44-6 CAPLUS  
 CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 8-(chloromethyl)-7,8-dihydro-1-methyl-4-(phenylmethoxy)-, 1,1-dimethylethyl ester, (8S)- (9CI) (CA INDEX NAME)

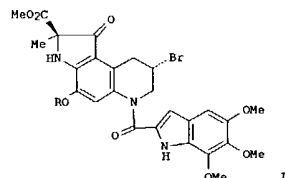
Absolute stereochemistry. Rotation (-).

L14 ANSWER 18 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RE.CWT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

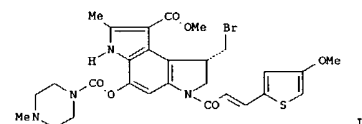
10/069,202

L14 ANSWER 19 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1999:716681 CAPLUS  
 DN 132:49819  
 TI Synthesis and antitumor activity of water-soluble duocarmycin B1 prodrugs  
 AU Asai, Akira; Nagamura, Satoru; Kobayashi, Eiji; Gomi, Katsushige; Saito, Hiromitsu  
 CS Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd, Machida, 194-8533, Japan  
 SO Bioorganic & Medicinal Chemistry Letters (1999), 9(20), 2995-2998  
 CODEN: BMCLE8; ISSN: 0960-894X  
 PB Elsevier Science Ltd.  
 DT Journal  
 LA English  
 GI



AB The water-soluble duocarmycin B1 prodrugs such as I (R =  $\beta$ -D-glucopyranosyl; [OH]2OP; N-methylpiperazinylcarbonyl) were synthesized for improving biol. and pharmaceutical profiles of duocarmycin. Among these prodrugs, I (R = N-methylpiperazinylcarbonyl) exhibited potent antitumor activity against several human tumors in vivo.  
 IT 171599-29-4P  
 RL BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent) (preparation and antitumor activity of water-soluble duocarmycin B1 prodrugs)  
 RN 171599-29-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-

L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1999:674932 CAPLUS  
 DN 132:22791  
 TI Synthesis and antitumor activity of duocarmycin derivatives: a-ring pyrrole compounds bearing 5-membered heteroarylacryloyl groups  
 AU Amishiro, Nobuyoshi; Nagamura, Satoru; Kobayashi, Eiji; Okamoto, Akihiko; Gomi, Katsushige; Saito, Hiromitsu  
 CS Pharmaceutical Research Institute, Kyowa Hakko Kogyo Company, Ltd., Shizuoka, 411-8731, Japan  
 SO Chemical & Pharmaceutical Bulletin (1999), 47(10), 1393-1403  
 CODEN: CPBTL5; ISSN: 0009-2363  
 PB Pharmaceutical Society of Japan  
 DT Journal  
 LA English  
 OS CASREACT 132:22791  
 GI

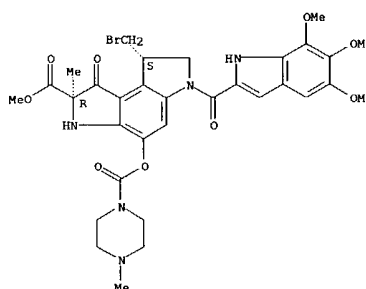


AB A series of A-ring pyrrole compds. of duocarmycin bearing 5-membered heteroarylacryloyl groups (thienylacryloyl and pyrrolylacryloyl) and heteroarylcarbonyl groups were synthesized and evaluated for in vitro anticellular activity against Hela S3 cells and in vivo antitumor activity against murine sarcoma 180 in mice. Most of the thienylacrylates displayed in vitro anticellular activity equivalent to 4'-methoxycinnamates. Among the 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of methoxy-thienylacrylates, compound I, having 4'-methoxy-2'-thienylacryloyl as segment-B (Seg-B), showed remarkably potent antitumor activity and low peripheral blood toxicity in vivo, which were equal to those of 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of 4'-methoxycinnamates, compared with the A-ring pyrrole derivs. having the trimethoxyindole skeleton in Seg-B. On the other hand, the 2'-pyrrolylacrylates having a double bond as spacer showed 102- to 103-fold stronger anticellular activity than 2'-pyrrolylacrylates (IC50<0.3 nM, 72h-exposure).  
 The 8-O-acetate and 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of 2'-pyrrolylacrylates exhibited an antitumor effect at a lower dose compared with the 8-O-[(N-methylpiperazinyl)carbonyl] derivs. with a

L14 ANSWER 19 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



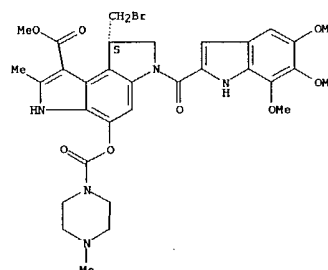
PAGE 2-A

● HCl

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 4'-methoxycinnamoyl moiety. Moreover, it was expected that the antitumor activity would be increased by the strength of the extra hydrogen bond formed between the nitrogen of the pyrrole amido group and DNA, owing to the increase of the no. of N-methyl-2'-pyrrolylacrylate units. However, 2'-pyrrolylacrylates having three N-methyl-2'-pyrrolylacrylate units showed nearly equal antitumor activity to 2'-pyrrolylacrylates having only one N-methyl-2'-pyrrolylacrylate unit.  
 IT 160819-28-3 186760-06-5  
 RL BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (synthesis and antitumor activity of duocarmycin derivs. bearing 5-membered heteroarylacryloyl groups)  
 RN 160819-28-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide, (8S)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry.

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PAGE 2-A

● HBr

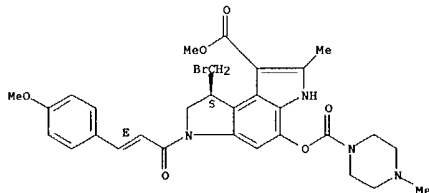
10/069,202

L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 186760-06-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(4-methyl-1-piperazinyl)carbonyl]oxy-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



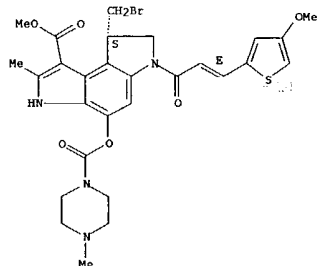
● HCl

IT 251999-64-1P 251999-94-7P 251999-95-8P  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation);  
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
 (synthesis and antitumor activity of duocarmycin derivs. bearing  
 5-membered heteroacylacryloyl groups)

RN 251999-64-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-  
 tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-{(2E)-1-  
 oxo-3-(2-thienyl)-2-propenyl}-, methyl ester, (8S)- (9CI) (CA INDEX  
 NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

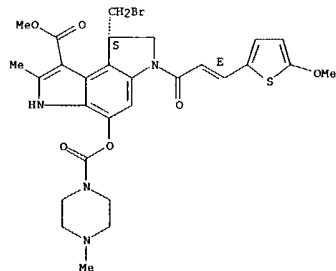
L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 251999-95-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

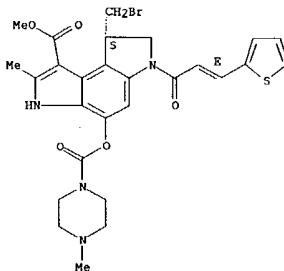
tetrahydro-6-[(2E)-3-(5-methoxy-2-thienyl)-1-oxo-2-propenyl]-2-methyl-4-  
[[4-methyl-1-piperazinyl]carbonyl]oxy-, methyl ester, (8S)- (9CI)  
(CA  
INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



IT 251999-68-5P 251999-73-2P 251999-74-3P

L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 251999-94-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(4-methoxy-2-thienyl)-1-oxo-2-propenyl]-2-methyl-4-  
[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)-(9CI)  
(CA  
INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

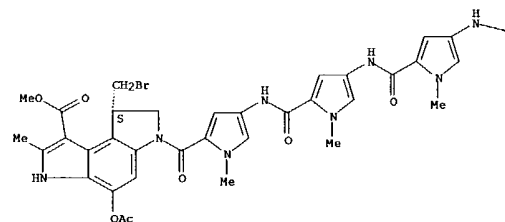
L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
251999-75-4P 251999-76-5P 251999-77-6P

RU: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(synthesis and antitumor activity of duocarmycin derivs. bearing 5-membered heteroarylacryloyl groups)

RN 251999-68-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(  
 bromomethyl)-6-[[4-[[[4-[[[4-[[[1,1-dimethylethoxy]carbonyl]amino]-1-  
 methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-  
 yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]-3,6,7,8-tetrahydro-2-  
 methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

**Absolute stereochemistry.**

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PAGE 1-B

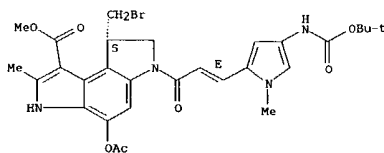


RN 251999-73-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-6-[[{(2E)-3-[4-[[{(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

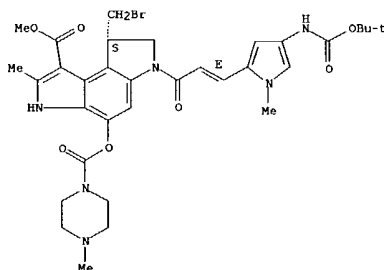
10/069,202

L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



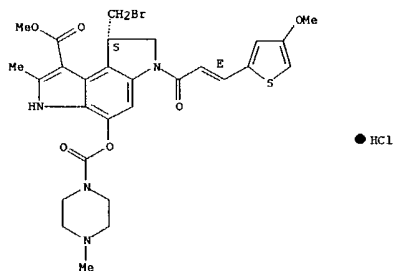
RN 251999-74-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-6-[(2E)-3-  
[4-[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-  
propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[(4-methyl-1-  
piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX  
NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



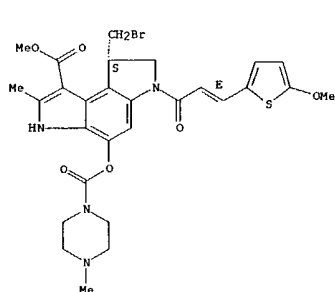
RN 251999-75-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-6-[(2E)-3-[(4-methoxy-2-thienyl)-1-oxo-2-propenyl]-2-methyl-4-  
[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(2E)-1-  
oxo-3-(2-thienyl)-2-propenyl]-, methyl ester, monohydrochloride,  
(8S)-

L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 251999-77-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-6-[(2E)-3-[(5-methoxy-2-thienyl)-1-oxo-2-propenyl]-2-methyl-4-  
[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester,  
monohydrochloride,  
(8S)- (9CI) (CA INDEX NAME)

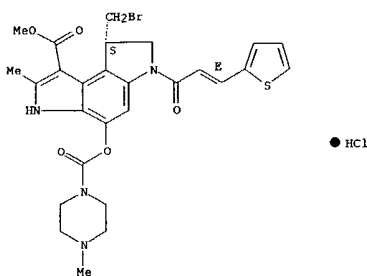
Absolute stereochemistry.  
Double bond geometry as shown.



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L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



RN 251999-76-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-[(4-methoxy-2-thienyl)-1-oxo-2-propenyl]-2-methyl-4-  
[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester,  
monohydrochloride,  
(8S)- (9CI) (CA INDEX NAME)

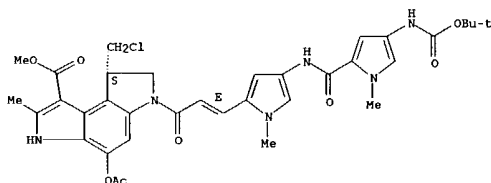
Absolute stereochemistry.  
Double bond geometry as shown.

L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A

RN 251999-82-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-  
(chloromethyl)-6-[(2E)-3-[4-[[[4-[(1,1-dimethylethoxy)carbonyl]amino]-1-  
methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-  
propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



RN 251999-83-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-  
(chloromethyl)-6-[(2E)-3-[4-[[[4-[(1,1-dimethylethoxy)carbonyl]amino]  
1-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-  
yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6,7,8-  
tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

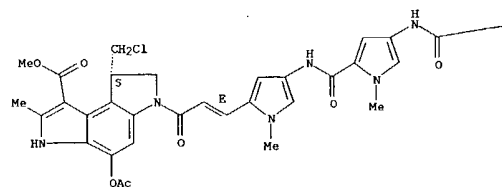
Absolute stereochemistry.  
Double bond geometry as shown.



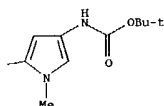
10/069,202

L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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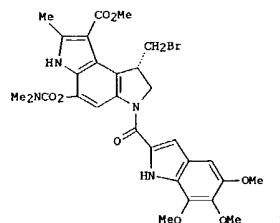
PAGE 1-B



RE.CMT 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 21 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

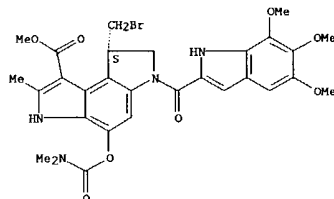
AN 1999:514023 CAPLUS  
DN 131:322456  
TI Antitumor antibiotics: duocarmycins  
AU Nagamura, Satoru; Saito, Hiromitsu  
CS Tokyo Research Laboratories, Kyowa Hakko Kogyo Co. Ltd., Tokyo, 194,  
Japan  
SO Chemistry of Heterocyclic Compounds (New York) (Translation of Khimiya  
Geterotsiklicheskikh Soedinenii) (1999), Volume Date 1998, 34(12),  
1386-1405  
CODEN: CHOCAL; ISSN: 0009-3122  
PB Consultants Bureau  
DT Journal  
LA English  
GI



AB Duocarmycin A-ring pyrrole derivs. e.g. I, were prepared from  
duocarmycin B2  
and B1 and were evaluated for antitumor activity. The IC50 of I  
against  
HeLa S3 cells was 55 nM. The antitumor activity and relationship  
between  
the phys. properties and biol. potency was studied.  
IT 177958-20-2  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological  
study, unclassified); RCT (Reactant); BIOL (Biological study); RACT  
(Reactant or reagent)  
(preparation and antitumor activity of duocarmycin derivs.)  
RN 177958-20-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-

L14 ANSWER 21 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
[[ (dimethylamino) carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester, (8S)- (9CI) (CA  
INDEX  
NAME)

Absolute stereochemistry.

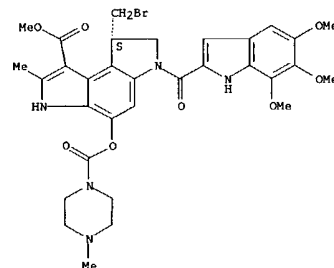


IT 154889-68-6P 160819-28-3P 177958-19-9P  
183240-24-6P 183240-25-7P  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological  
study, unclassified); SPN (Synthetic preparation); BIOL (Biological  
study); PREP (Preparation)  
(preparation and antitumor activity of duocarmycin derivs.)  
RN 154889-68-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[ (4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester, (8S)- (9CI) (CA  
INDEX  
NAME)

Absolute stereochemistry.

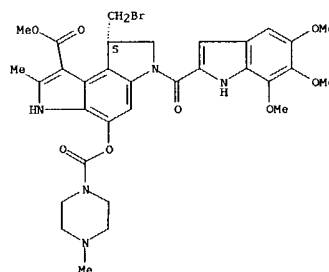
L14 ANSWER 21 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 160819-28-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-2-methyl-4-[[ (4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester, monohydrobromide,  
(8S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

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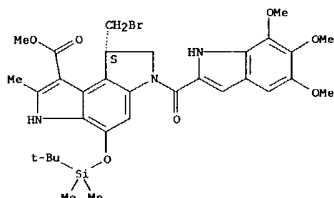
L14 ANSWER 21 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A

● HBr

RN 177958-19-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-4-[[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



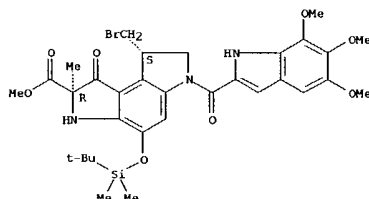
RN 183240-24-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[(1-piperidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 21 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

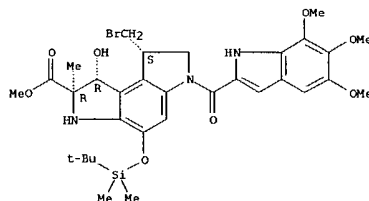
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
 8-(bromomethyl)-4-[[[1,1-dimethylethyl]dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



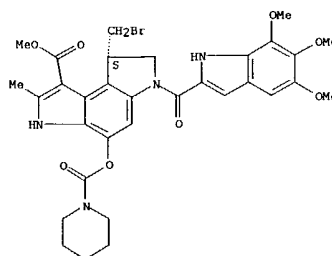
RN 129953-17-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
 8-(bromomethyl)-4-[[[1,1-dimethylethyl]dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R,2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



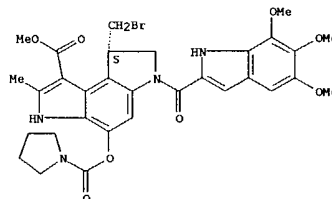
RN 183388-25-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
 8-(bromomethyl)-4-[[[1,1-

L14 ANSWER 21 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 183240-25-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[(1-pyrrolidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

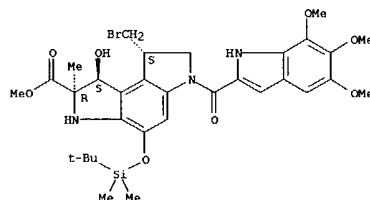


IT 129953-15-7P 129953-17-9P 183388-25-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (preparation and antitumor activity of duocarmycin derivs.)  
 RN 129953-15-7 CAPLUS

L14 ANSWER 21 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

dimethylethyl]dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R,2S,8S)- (9CI) (CA INDEX NAME)

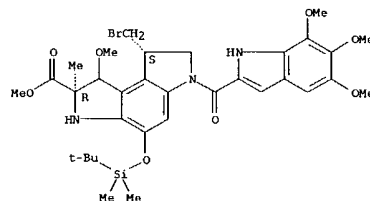
Absolute stereochemistry.



IT 248246-16-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and antitumor activity of duocarmycin derivs.)  
 RN 248246-16-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
 8-(bromomethyl)-4-[[[1,1-

dimethylethyl]dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

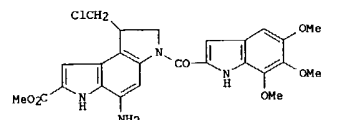
Absolute stereochemistry.



RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 21 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

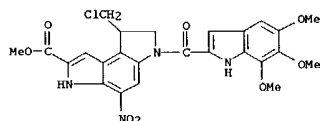
L14 ANSWER 22 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1999:439196 CAPLUS  
 DN 131:286298  
 TI Synthesis and Cytotoxicity of Amino-seco-DSA: An Amino Analogue of the DNA Alkylating Agent Duocarmycin SA  
 AU Tercel, Moanar Gieseg, Michael A.; Denny, William A.; Wilson, William R.  
 CS Auckland Cancer Society Research Centre Faculty of Medicine and Health Science, The University of Auckland, Auckland, 92019, N. Z.  
 SO Journal of Organic Chemistry (1999), 64(16), 5946-5953  
 CODEN: JOCEAH; ISSN: 0022-3263  
 PB American Chemical Society  
 DT Journal  
 LA English  
 OS CASREACT 131:286298  
 GI



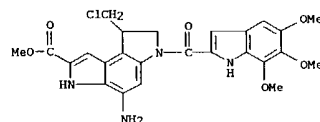
AB This paper describes the synthesis of Me 5-amino-1-(chloromethyl)-3-[(5,6,7-trimethoxyindol-2-yl)carbonyl]-1,2-dihydro-3H-pyrrolo[3,2-e]indole-7-carboxylate (I), an amino analog of the anticancer antibiotic and potent DNA minor groove alkylating agent seco-duocarmycin SA. Key points in the synthesis are sequential radical cyclization and Hunsdiecker reaction steps to construct the indoline and indole rings of the target compound from a 1,2,3-trisubstituted benzene precursor. An intermediate has been resolved by chiral chromatog. to provide the sep. enantiomers of I. Racemic I alkylates DNA at adenine in AT rich sequences, similar to seco-duocarmycin SA and the previously reported amino-seco-CBI, but is 15-60 times less potent in an in vitro cytotoxicity test. Derivs. of I in which the amino group is replaced by an electron-withdrawing nitro or nitrobenzylcarbamate substituent are considerably less toxic and may have application as prodrugs to be activated selectively in a tumor environment.  
 IT 204915-56-0P 204915-57-1P 204915-59-3P

L14 ANSWER 22 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

204915-60-6P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent) (synthesis and cytotoxicity of amino-seco-DSA, prep. of amino analog of DNA alkylating agent duocarmycin SA)  
 RN 204915-56-0 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-nitro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

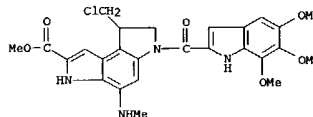


RN 204915-57-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 4-amino-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

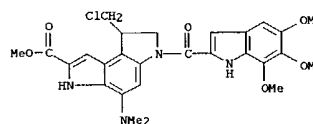


RN 204915-59-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-(methylamino)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 22 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



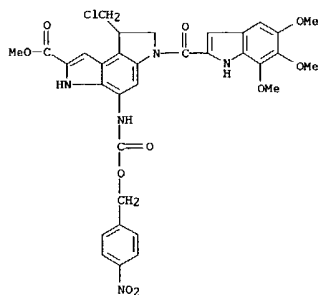
RN 204915-60-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-4-(dimethylamino)-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



IT 204915-61-7P 246137-60-0P 246137-61-1P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (synthesis and cytotoxicity of amino-seco-DSA, preparation of amino analog of DNA alkylating agent duocarmycin SA)  
 RN 204915-61-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[4-(nitrophenyl)methoxy]carbonyl]amino]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

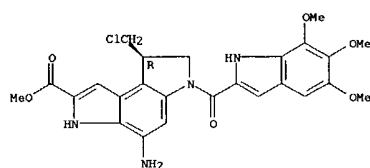
10/069,202

L14 ANSWER 22 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



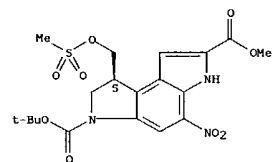
RN 246137-60-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 4-amino-8-(chloromethyl)-, 6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

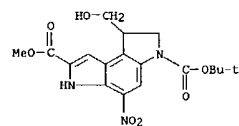


RN 246137-61-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 4-amino-8-(chloromethyl)-, 6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8R)- (9CI) (CA INDEX NAME)

L14 ANSWER 22 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



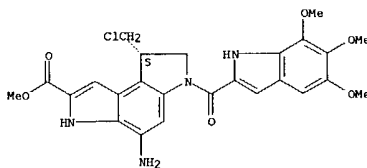
IT 204916-10-9P 204916-11-0P 246137-52-0P  
246137-56-4P 246137-57-5P 246137-58-6P  
246137-59-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT (Reactant or reagent)  
(synthesis and cytotoxicity of amino-seco-DSA, preparation of  
amino analog  
of DNA alkylating agent duocarmycin SA)  
RN 204916-10-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-8-[(hydroxymethyl)-4-nitro-, 6-(1,1-dimethylethyl) 2-methyl ester (9CI) (CA INDEX NAME)



RN 204916-11-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-4-nitro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

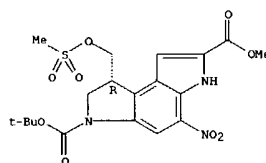
L14 ANSWER 22 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 246137-54-2P 246137-55-3P  
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(synthesis and cytotoxicity of amino-seco-DSA, preparation of  
amino analog  
of DNA alkylating agent duocarmycin SA)  
RN 246137-54-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-8-[(methylsulfonyl)oxymethyl]-4-nitro-, 6-(1,1-dimethylethyl) 2-methyl ester, (8R)- (9CI) (CA INDEX NAME)

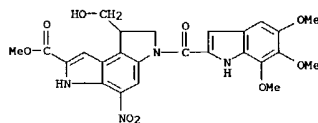
Absolute stereochemistry.



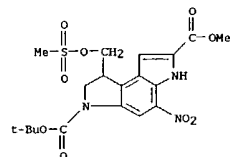
RN 246137-55-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-8-[(methylsulfonyl)oxymethyl]-4-nitro-, 6-(1,1-dimethylethyl) 2-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

L14 ANSWER 22 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

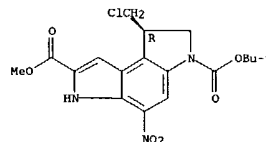


RN 246137-52-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-8-[(methylsulfonyl)oxymethyl]-4-nitro-, 6-(1,1-dimethylethyl) 2-methyl ester (9CI) (CA INDEX NAME)



RN 246137-56-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-nitro-, 6-(1,1-dimethylethyl) 2-methyl ester, (8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

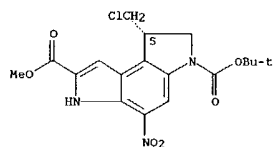


RN 246137-57-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-nitro-, 6-(1,1-dimethylethyl) 2-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

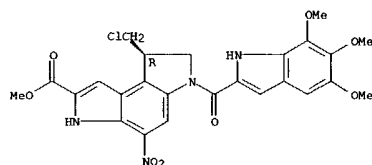
10/069,202

L14 ANSWER 22 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 246137-58-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-4-nitro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,  
methyl  
ester, (8R)- (9CI) (CA INDEX NAME)

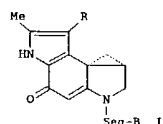
Absolute stereochemistry. Rotation (-).



RN 246137-59-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-4-nitro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,  
methyl  
ester, (8S)- (9CI) (CA INDEX NAME)

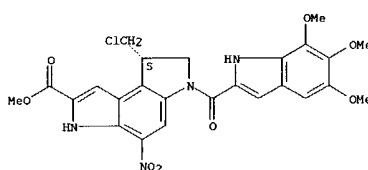
Absolute stereochemistry. Rotation (+).

L14 ANSWER 23 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1999:431081 CAPLUS  
DN 131:286297  
TI Synthesis and Antitumor Activity of Duocarmycin Derivatives:  
Modification  
of Segment-A of A-Ring Pyrrole Compounds  
AU Amishiro, Nobuyoshi; Okamoto, Akihiko; Murakata, Chikara; Tamaoki,  
Tatsuya; Okabe, Masami; Saito, Hiromitsu  
CS Pharmaceutical Research Institute, Kyowa Hakko Kogyo Company Ltd.,  
Nagatsumi Sunto Shizuoka, 411-8731, Japan  
SO Journal of Medicinal Chemistry (1999), 42(15), 2946-2950  
CODEN: JMCMAH ISSN: 0022-2623  
PB American Chemical Society  
DT Journal  
LA English  
GI

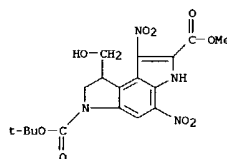


AB A series of 3-substituted A-ring pyrrole compds. of duocarmycin were  
synthesized and evaluated for in vitro anticellular activity against  
HeLa  
S3 cells and in vivo antitumor activity against murine sarcoma 180 in  
mice. These compds. were evaluated for peripheral blood toxicity and  
delayed lethal toxicity. Further, to expand the investigation of  
their  
peripheral blood toxicity, the toxicity to bone marrow cells (CFU-GM,  
CFU-Meg) was investigated. Among 3-substituted A-ring pyrrole  
compds. of  
duocarmycin bearing a 5',6',7'-trimethoxy-2'-indolecarboxyl (Q)  
group as  
segment-B, several analogs showed remarkably potent antitumor  
activity  
with low peripheral blood toxicity. The 3-formyl compound I [R =  
CHO, seg-B  
= Q] showed stronger antitumor activity with lower toxicity to bone  
marrow  
cells than DU-86, an active metabolite of KW-2189. However, this  
compound  
caused delayed death. On the other hand, the 3-bromo compound I [R  
= Br,  
seg-B = 4-methoxycinnamoyl] showed the most potent antitumor activity  
among the 4'-methoxycinnamate analogs with low toxicity to bone  
marrow  
cells. Furthermore, this compound did not cause delayed death.  
These

L14 ANSWER 22 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



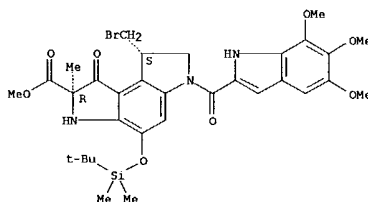
IT 246137-63-3P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(synthesis and cytotoxicity of amino-seco-USA, preparation of  
amino analog  
of DNA alkylating agent duocarmycin SA)  
RN 246137-63-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,  
7,8-dihydro-8-(hydroxymethyl)-1,4-dinitro-, 6-(1,1-dimethylethyl)-  
2-methyl  
ester (9CI) (CA INDEX NAME)



RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 23 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
results would indicate the importance of the C-3 substituents of  
A-ring  
pyrrole duocarmycin derivs. for exhibiting antitumor activity and  
decreasing toxicity.  
IT 129953-15-7 177958-19-9 246034-79-7  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation and antitumor activity of duocarmycin derivs. with  
modified  
segment-A)  
RN 129953-15-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(bromomethyl)-4-[[[1,1-  
dimethylethyl]dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-  
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-  
(9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

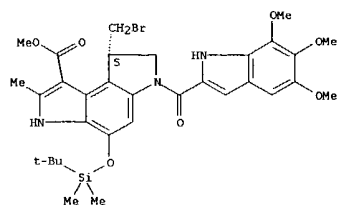


RN 177958-19-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[[[1,1-  
dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA  
INDEX  
NAME)

Absolute stereochemistry.

10/069,202

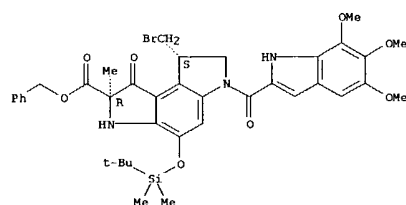
L14 ANSWER 23 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 246034-79-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-  
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, phenylmethyl ester,  
(2R,8S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 205050-84-6P 205051-09-8P 205051-11-2P  
205051-57-6P 205051-58-7P 246034-75-3P  
246034-76-4P 246034-77-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

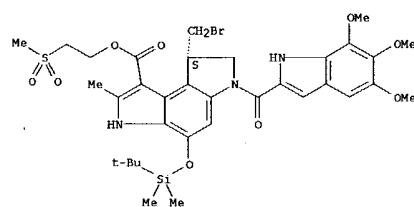
RACT  
(Reactant or reagent)  
(preparation and antitumor activity of duocarmycin deriva. with  
modified  
segment-A)

L14 ANSWER 23 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 205051-11-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl)carbonyl]-, 2-(methylsulfonyl)ethyl ester,  
(8S)- (9CI) (CA INDEX NAME)

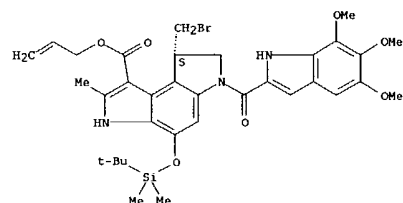
Absolute stereochemistry.



RN 205051-57-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester, (8S)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



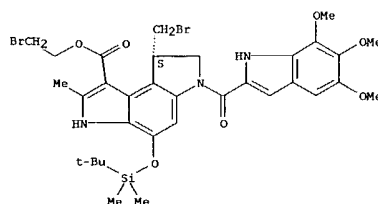
RN 205051-58-7 CAPLUS

L14 ANSWER 23 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 205050-84-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl)carbonyl]-, 2-bromoethyl ester, (8S)- (9CI)  
(CA INDEX NAME)

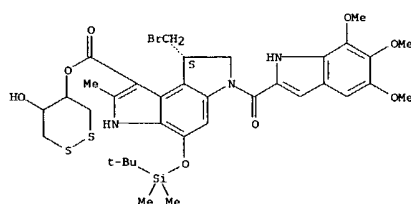
Absolute stereochemistry.



RN 205051-09-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl)carbonyl]-, 5-hydroxy-1,2-dithian-4-yl ester,  
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

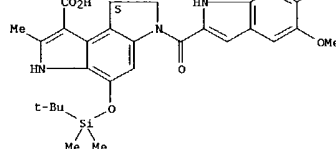


L14 ANSWER 23 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 205051-11-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl)carbonyl]-, (8S)- (9CI) (CA INDEX NAME)

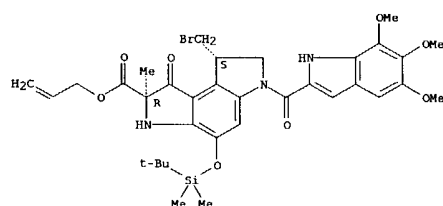
Absolute stereochemistry.



RN 246034-75-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-  
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester,  
(2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



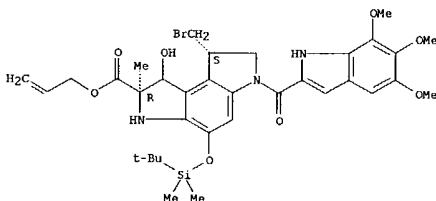
RN 246034-76-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-

10/069,202

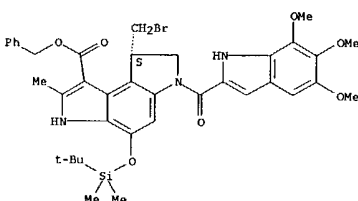
L14 ANSWER 23 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
6-[[5,6,7-trimethoxy-1H-indol-2-yl]carbonyl]-, 2-propenyl ester,  
(2R,8S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 246034-77-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[[1,1-dimethylethyl]dimethylsilyloxy]-3,6,7,8-tetrahydro-2-methyl-6-[[5,6,7-trimethoxy-1H-indol-2-yl]carbonyl]-, phenylmethyl ester, (8S)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



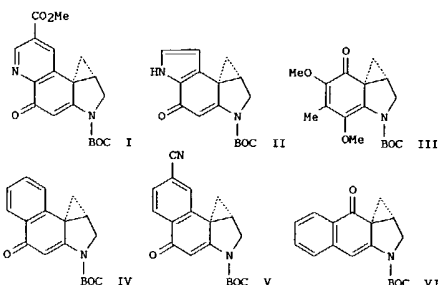
RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 24 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1999:308148 CAPLUS  
DN 131:44697  
TI Synthesis of CC-1065/duocarmycin analogs  
IN Boger, Dale L.  
PA The Scripps Research Institute, USA  
SO PCT Int. Appl., 36 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

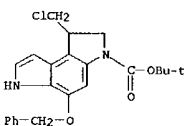
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9929642	A1	19990617	WO 1998-US25992	19981208
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TH, RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CH, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2313231	AA	19990617	CA 1998-2313231	19981208
AU 9918079	A1	19990628	AU 1999-18079	19981208
EP 1037865	A1	20000927	EP 1998-962954	19981208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001525382	T2	20011211	JP 2000-524241	19981208
NZ 504884	A	20021025	NZ 1998-504884	19981208
NO 2000002900	A	20000808	NO 2000-2900	20000607
US 6310209	B1	20011030	US 2000-581049	20000710
US 2002082424	A1	20020627	US 2001-1611	20011030
US 1997-67960P	P	19971208		
WO 1998-US25992	W	19981208		
US 2000-581049	A3	20000710		
CASREACT 131:44697				

L14 ANSWER 23 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L14 ANSWER 24 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



AB The dihydroindole C-ring found in CC-1065/duocarmycin analogs is formed by the 5-exo-trig radical cyclization of an aryl halide onto a tethered vinyl chloride forming with chlorine installed as a suitable leaving group for subsequent cyclopropane spirocyclization. The versatility of this approach is disclosed in the context of six CC-1065/duocarmycin analogs (I-VI) previously synthesized in this laboratory  
IT 227084-68-5P  
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (process for the synthesis of CC-1065/duocarmycin analogs)  
RN 227084-68-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 24 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

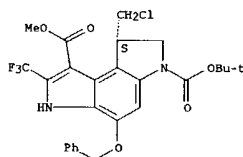
L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1999:210305 CAPLUS  
 DN 130:338038  
 TI Novel cyclopropapyrroloindole derivative (AT-3510) bearing methoxycarbonyl and trifluoromethyl groups  
 AU Fukuda, Yasumichi; Furuta, Hirotsuke; Kusama, Yoshie; Ebisu, Hiroyuki; Oomori, Yasuo; Terashima, Shiro  
 CS Central Research Laboratories, Kyorin Pharmaceutical Company Ltd., Mitairai  
 NOgi Tochigi, 329-0114, Japan  
 SO Journal of Medicinal Chemistry (1999), 42(8), 1448-1458  
 CODEN: JMCMAH; ISSN: 0022-2623  
 PB American Chemical Society  
 DT Journal  
 LA English  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The seco-C1 3-methoxycarbonyl-2-trifluoromethylcyclopropapyrroloindole (MCTFCPI) derivs. dl- and/or (S)-I [Ar = Q, Q1, Q2, Q3, R = 4,5,6-(MeO)3, 5,6,7-(MeO)3, 5-MeO, etc., X = NH, O, CH, Y = CH, N] carrying various acyl moieties at the N6-position were synthesized along with their prodrugs (S)-II, and their antitumor activity was evaluated. Among these derivs., AT-3510 [(S)-II (Ar = Q1, R = 7-MeO, X = O)], the novel prodrug MCTFCPI derivative carrying a 5-(7-methoxybenzofuran-2-ylcarbonyl)aminoindole-2-carbonyl group at the N6-position, was found to exhibit more excellent antitumor activity against human tumor xenografts than the clin. trial candidates carzelesin and KW-2189 (III) and cisplatin.  
 IT 157823-12-6P 157904-26-2P 157904-27-3P  
 194093-62-4P 194093-63-5P 194093-64-6P  
 224321-50-0P 224321-51-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (intermediate in preparation, antitumor activity, and cytotoxicity of pyrroloindole derivs.)  
 RN 157823-12-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

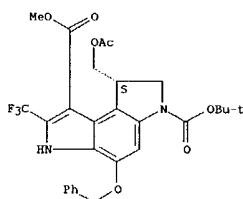
Absolute stereochemistry. Rotation (-).

L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 157904-26-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

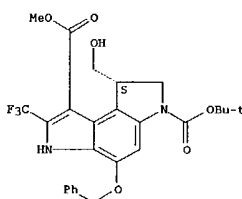
Absolute stereochemistry. Rotation (-).



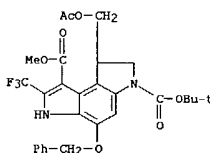
RN 157904-27-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

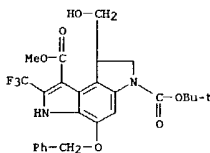
L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 194093-62-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



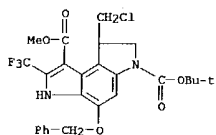
RN 194093-63-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)





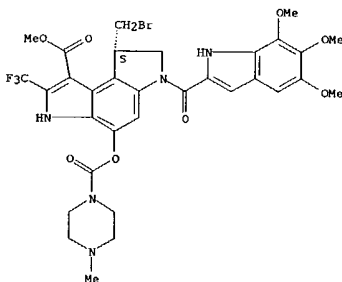
10/069,202

L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 RN 194093-64-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-,  
 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



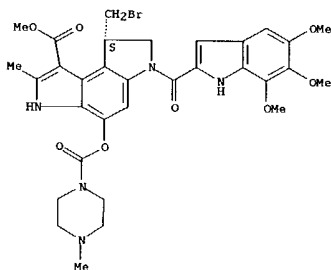
RN 224321-50-0 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-  
 tetrahydro-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-6-  
 -[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-  
 trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.

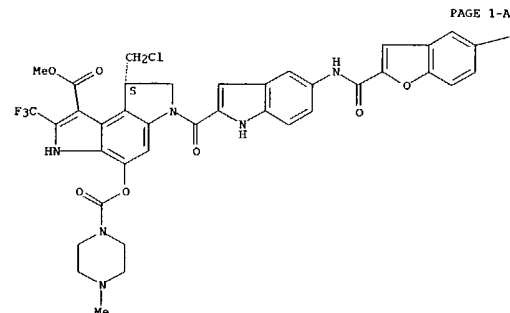


IT 157823-41-1P 157823-42-2P 157823-43-3P  
 157823-45-5P 157904-34-2P 194361-61-0P  
 224321-52-2P  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (preparation, antitumor activity, and cytotoxicity of pyrroloindole derivs.)  
 RN 157823-41-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-3,6,7,8-  
 tetrahydro-6-[[5-[[[(5-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 RN 224321-51-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-3,6,7,8-  
 tetrahydro-6-[[5-[[[(5-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

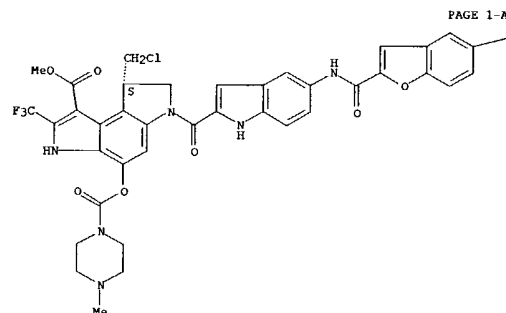


PAGE 1-A

OMe  
 IT 154889-68-6, KW-2189  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological study, unclassified); BIOL (Biological study)  
 (preparation, antitumor activity, and cytotoxicity of pyrroloindole derivs.)  
 RN 154889-68-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-

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L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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OMe  
 PAGE 1-B

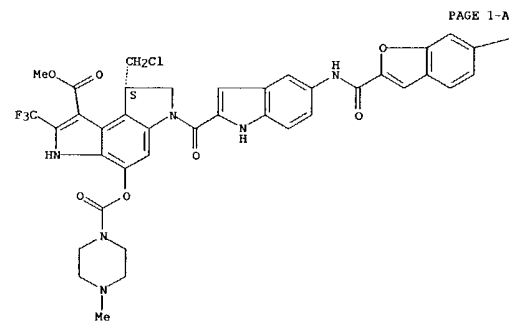
● HCl

RN 157823-42-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-3,6,7,8-  
 tetrahydro-6-[[5-[[[(6-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

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L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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OMe

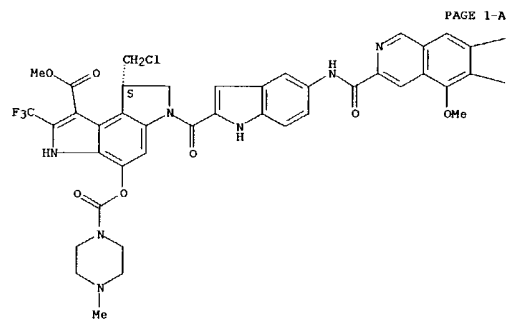
● HCl

RN 157823-43-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-6-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-  
6-[[[5-[[[(5,6,7-trimethoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA  
INDEX

L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 157823-45-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-6-  
[[[5-[[[(5,6,7-trimethoxy-3-isoquinoliny]carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry. Rotation (+).



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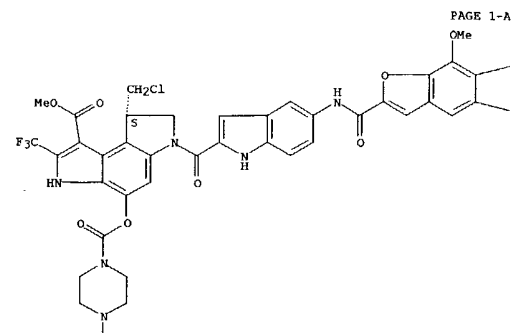
OMe

OMe

● HCl

L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry. Rotation (+).



PAGE 1-B

OMe

OMe

Me

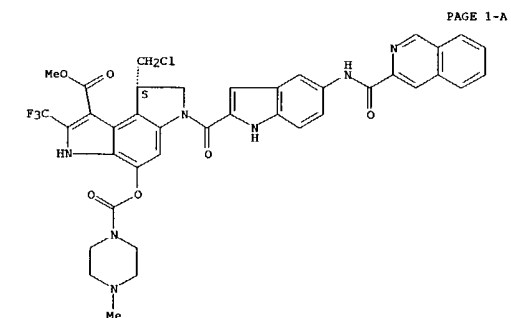
PAGE 2-A

● HCl

L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 157904-34-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-6-[[[5-[(3-isoquinoliny]carbonyl]amino]-1H-indol-2-yl]carbonyl]-  
4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-, methyl  
ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



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● HCl

RN 194361-61-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

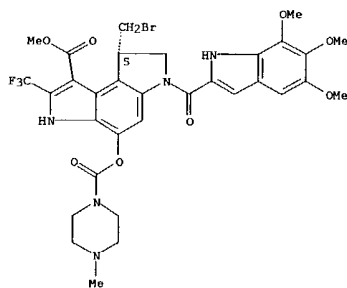
tetrahydro-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-6-  
[[[5,6,7-trimethoxy-1H-indol-2-yl]carbonyl]-, methyl ester,  
monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

10/069,202

L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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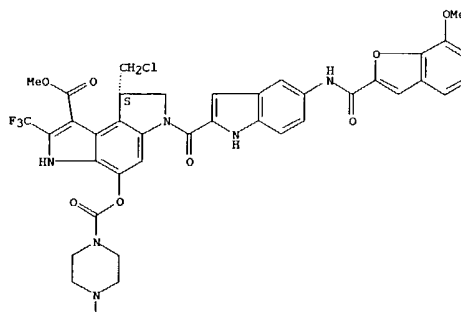
PAGE 2-A

● HCl

RN 224321-52-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-6-[[5-[[7-methoxy-2-benzofuranyl]carbonyl]amino]-1H-indol-2-  
yl]carbonyl]-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-2-(trifluoromethyl)-  
methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)  
Absolute stereochemistry. Rotation (+).

L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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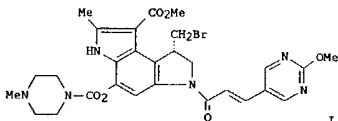


PAGE 2-A

● HCl

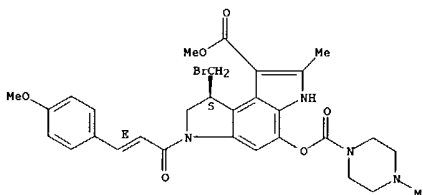
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 26 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1999:73220 CAPLUS  
DN 130:252170  
TI New Water-Soluble Duocarmycin Derivatives: Synthesis and Antitumor  
Activity of A-Ring Pyrrole Compounds Bearing  $\beta$ -Heteroarylacryloyl  
Groups  
AU Amishiro, Nobuyoshi; Nagamura, Satoru; Kobayashi, Eiji; Gomi,  
Katsushige;  
Saito, Hiromitsu  
CS Pharmaceutical Research Institute, Kyowa Hakko Kogyo Company Ltd.,  
Nagaizumi, Sunto Shizuoka, 411-0943, Japan  
SO Journal of Medicinal Chemistry (1999), 42(4), 669-676  
CODEN: JMCMAH; ISSN: 0022-2623  
PB American Chemical Society  
DT Journal  
LA English  
GI



AB A series of A-ring pyrrole compds. of duocarmycin bearing  
4'-methoxy- $\beta$ -heteroarylacryloyl groups were synthesized and  
evaluated  
for in vitro anticellular activity against HeLa S3 cells and in vivo  
antitumor activity against murine sarcoma 180 in mice. Most of the  
4'-methoxy- $\beta$ -heteroarylacrylates displayed in vitro anticellular  
activity equivalent to that of 4'-methoxycinnamates. Among the  
8-O-[(N-methylpiperazinyl)carbonyl] derivs. of 4'-methoxy- $\beta$ -  
heteroarylacrylates, compound 1-HCl having a (4-methoxy-3,5-  
pyrimidinyl)acryloyl as segment-B (Seg-B) showed remarkably potent  
in vivo  
antitumor activity and low peripheral blood toxicity compared with  
the  
A-ring pyrrole derivs. having the trimethoxyindole skeleton in Seg-B,  
which were equal to 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of  
4'-methoxycinnamates. Moreover, these  
8-O-[(N-methylpiperazinyl)carbonyl]  
derivs. of 4'-methoxy- $\beta$ -heteroarylacrylates had high aqueous  
solubility.  
IT 186760-19-0  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological  
study, unclassified); BIOL (Biological study)  
(synthesis and antitumor activity of  $\beta$ -heteroarylacryloyl group

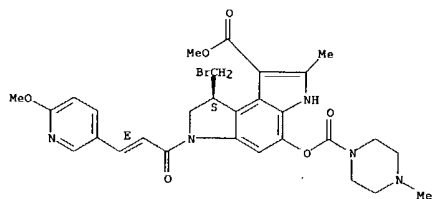
L14 ANSWER 26 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
bearing pyrrole analogs of duocarmycin)  
RN 186760-19-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-  
methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA  
INDEX  
NAME)  
Absolute stereochemistry.  
Double bond geometry as shown.



IT 221549-89-9P 221549-92-4P 221549-95-7P  
221549-99-1P  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological  
study, unclassified); SPN (Synthetic preparation); BIOL (Biological  
study); PREP (Preparation)  
(synthesis and antitumor activity of  $\beta$ -heteroarylacryloyl group  
bearing pyrrole analogs of duocarmycin)  
RN 221549-89-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-6-[(2E)-3-(6-methoxy-3-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-  
[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester,  
monohydrochloride,  
(8S)- (9CI) (CA INDEX NAME)  
Absolute stereochemistry.  
Double bond geometry as shown.

10/069,202

L14 ANSWER 26 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

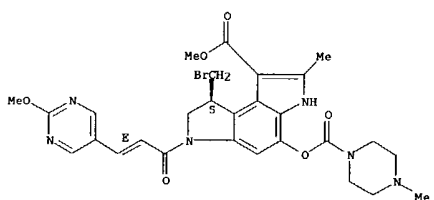


● HCl

RN 221549-92-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

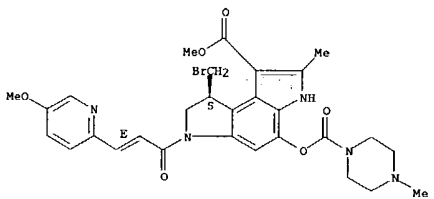
tetrahydro-6-[(2E)-3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyloxy]-, methyl ester,  
monohydrochloride, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



● HCl

L14 ANSWER 26 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



● HCl

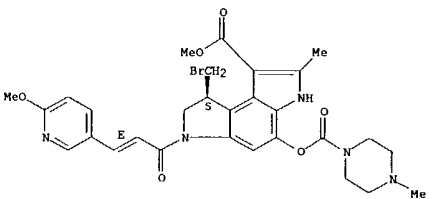
IT 221549-88-8P 221549-91-3P 221549-94-6P  
221549-98-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT (Reactant or reagent)  
(synthesis and antitumor activity of  $\beta$ -heteroarylacryloyl group  
bearing pyrrole analogs of duocarmycin)

RN 221549-88-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(6-methoxy-3-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyloxy]-, methyl ester, (8S)-(9CI)  
(CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

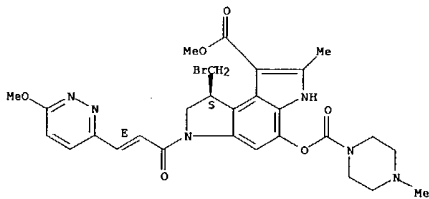


L14 ANSWER 26 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 221549-95-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(6-methoxy-3-pyridazinyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyloxy]-, methyl ester,  
monohydrochloride, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



● HCl

RN 221549-99-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(5-methoxy-2-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyloxy]-, methyl ester,  
monohydrochloride, (8S)-(9CI) (CA INDEX NAME)

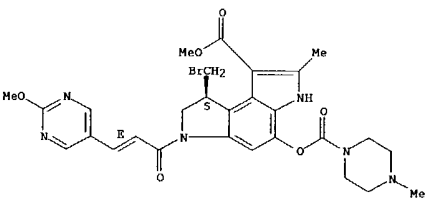
Absolute stereochemistry.  
Double bond geometry as shown.

L14 ANSWER 26 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 221549-91-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyloxy]-, methyl ester, (8S)-(9CI)  
(CA INDEX NAME)

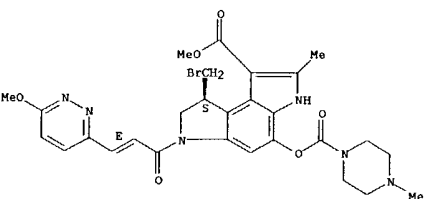
Absolute stereochemistry.  
Double bond geometry as shown.



RN 221549-94-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(6-methoxy-3-pyridazinyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyloxy]-, methyl ester, (8S)-(9CI)  
(CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



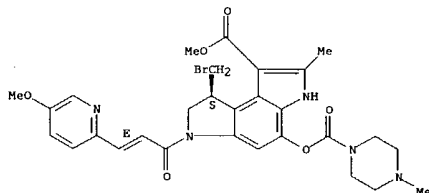
10/069,202

L14 ANSWER 26 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 221549-98-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(5-methoxy-2-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-  
[[4-methyl-1-piperazinyl]carbonyloxy]-, methyl ester, (8S)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

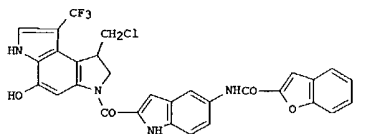


RE.CNT 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 27 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:32649 CAPLUS  
DN 130:168271

TI Synthesis and cytotoxicity of various structural types of novel  
cyclopropapyrroloindole (CPI) derivatives  
AU Fukuda, Yasumichi; Furuta, Hirotsugu; Kusama, Yoshie; Ebisu, Hiroyuki;  
Omoroi, Yasuo; Terashima, Shiro  
CS Central Research Laboratories, Kyorin Pharmaceutical Co. Ltd, Nogi,  
Tochigi, 329-0114, Japan  
SO Heterocycles (1998), 49, 53-58  
CODEN: HETCYAM; ISSN: 0385-5414  
PB Japan Institute of Heterocyclic Chemistry  
UT Journal  
LA English  
GI



AB Various structural types of novel cyclopropapyrroloindole (CPI)  
derivs.,

e.g. 1, were synthesized and their cytotoxicity was evaluated.

IT 132628-62-7 176685-39-5

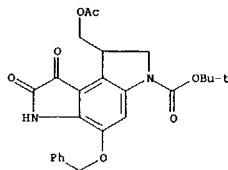
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation and antitumor activity of cyclopropapyrroloindole  
derivs.)

RN 132628-62-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
1-[(acetyloxy)methyl]-

1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl  
ester  
(9CI) (CA INDEX NAME)

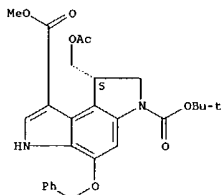
L14 ANSWER 27 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 176685-39-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-  
dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 176539-80-3P 176685-40-8P 176685-41-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT (Reactant or reagent)

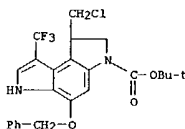
(preparation and antitumor activity of cyclopropapyrroloindole  
derivs.)

RN 176539-80-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
1-(chloromethyl)-1,6-

dihydro-5-(phenylmethoxy)-8-(trifluoromethyl)-, 1,1-dimethylethyl  
ester  
(9CI) (CA INDEX NAME)

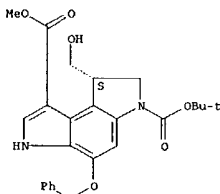
L14 ANSWER 27 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 176685-40-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-  
dimethylethyl)  
1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

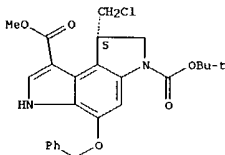
Absolute stereochemistry. Rotation (-).



RN 176685-41-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-  
dimethylethyl)  
1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



10/069,202

L14 ANSWER 27 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

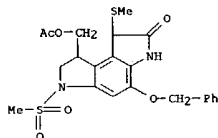
L14 ANSWER 28 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1998:721711 CAPLUS  
DW 130:4029  
TI Triplex forming oligonucleotides including pyrazolo(3,4-d)pyrimidine bases  
IN Meyer, Rich B.; Gall, Alexander; Kutayavin, Igor V.  
PA Epoch Pharmaceuticals, Inc., USA  
SO PCT Int. Appl., 65 pp.  
CODEN: PIXXU2  
DT Patent  
LA English  
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849180	A1	19981105	WO 1998-US8373	19980429
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, FI, GE, GH, GM, GW, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6143877	A	20001107	US 1997-848373	19970430
AU 9872586	A1	19981124	AU 1998-72586	19980429
PRAI US 1997-848373	A	19970430		
WO 1998-US8373	W	19980429		

AB A triplex forming oligonucleotide is complementary pursuant to the G/T or A/G recognition motif to a homopurine, or substantially homopurine target sequence in double stranded nucleic acids, and at least one and preferably all of the guanine bases are replaced by their pyrazolo[3,4-d]pyrimidine analog, namely by 6-amino-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one. The oligodeoxycytidyl nucleotides containing the pyrazolo[3,4-d]pyrimidine analog of guanine exhibit a lesser degree of self-association, and lack the nucleophilic nitrogen atom in the 7 position of guanine. The latter feature results in a diminished extent of self-crosslinking in ODNs which also have a covalently attached crosslinking agent.

IT 112089-53-9  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(triplex forming oligodeoxycytidyl nucleotides including pyrazolopyrimidine

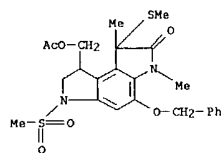
L14 ANSWER 28 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
base(s)  
RN 112089-53-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrol-2(1H)-one, 8-[(acetyloxy)methyl]-3,6,7,8-tetrahydro-6-(methylsulfonyl)-1-(methylthio)-4-(phenylmethoxy)-(9CI) (CA INDEX NAME)



IT 192657-40-2P 192657-42-4P 192657-43-5P  
215595-79-2P 215595-80-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT (Reactant or reagent)  
(triplex forming oligodeoxycytidyl nucleotides including pyrazolopyrimidine bases)

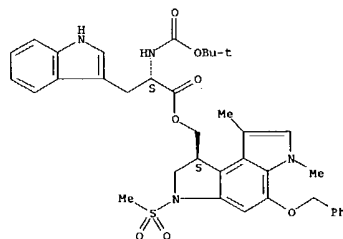
RN 192657-40-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrol-2(1H)-one, 8-[(acetyloxy)methyl]-3,6,7,8-tetrahydro-1,3-dimethyl-6-(methylsulfonyl)-1-(methylthio)-4-(phenylmethoxy)-(9CI) (CA INDEX NAME)



RN 192657-42-4 CAPLUS  
CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [(1S)-1,2,3,6-tetrahydro-6,8-dimethyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester (9CI) (CA INDEX NAME)

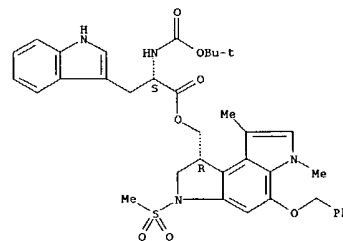
Absolute stereochemistry.

L14 ANSWER 28 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 192657-43-5 CAPLUS  
CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [(1R)-1,2,3,6-tetrahydro-6,8-dimethyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

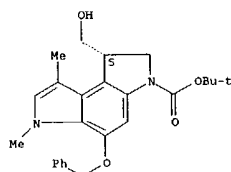


RN 215595-79-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-6,8-dimethyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

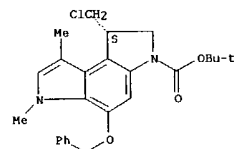
10/069,202

L14 ANSWER 28 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)



RN 215595-80-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
1-(chloromethyl)-1,6-  
dihydro-6,8-dimethyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester,  
(1S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

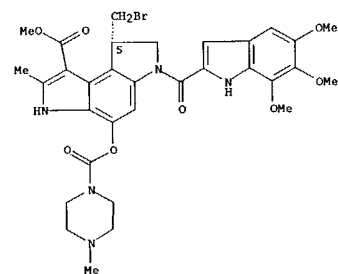
L14 ANSWER 29 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)  
effector, except adverse); BPR (Biological process); BSU (Biological  
study, unclassified); THU (Therapeutic use); BIOL (Biological  
study); PROC (Process); USES (Uses)

(duocarmycin semisynthetic deriv. KW-2189 toxicity and efficacy  
against chemotherapy-refractory solid tumors in humans)

RN 154889-68-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 29 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN

AN 1998:674015 CAPLUS  
DN 130:75837  
TI Phase I study of the duocarmycin semisynthetic derivative KW-2189  
given

daily for five days every six weeks  
AU Alberts, Steven R.; Erlichman, Charles; Reid, Joel M.; Sloan, Jeff A.;  
Ames, Matthew M.; Richardson, Ronald L.; Goldberg, Richard M.  
CS Divisions of Medical Oncology, Mayo Clinic, Rochester, MN, 55905, USA  
SO Clinical Cancer Research (1998), 4(9), 2111-2117

CODEN: CCRF4; ISSN: 1078-0432  
PB American Association for Cancer Research  
DT Journal  
LA English

AB The duocarmycins represent a new group of antitumor antibiotics  
produced  
by Streptomyces that bind to the minor groove of DNA. KW-2189 is a  
water-soluble semisynthetic derivative of duocarmycin B2, with  
significant  
activity in murine and human tumor models. We conducted a Phase I  
trial  
of KW-2189 in patients who had solid tumors that were refractory to  
standard  
chemotherapy or for whom no more effective therapy existed. KW-2189

was  
administered as a rapid i.v. bolus daily for 5 days every 6 wk.  
Twenty-two patients were enrolled and received a total of 31 cycles of  
KW-2189. Leukopenia, neutropenia, and thrombocytopenia were the  
dose-limiting toxicities, with nadirs occurring at medians of 36, 38,  
and  
29 days, resp., at the 0.04 mg/m2/day dose level. Nonhematol.

toxicities  
were mild, although one patient developed grade 3 fatigue. Four  
patients  
had stable disease over two to four cycles of treatment and showed no  
cumulative toxicity. The mean t1/2, plasma clearance, and  
steady-state  
volume of distribution were 13.5 min, 1,287 mL/min/m2, and 10,638  
mL/m2,

resp. Pharmacokinetics were similar on days 1 and 5, with no drug  
accumulation in plasma. The active metabolite DU-86 was not  
consistently  
found in patient plasma. For Phase II trials, when the 5 days every  
6 wk  
schedule was used, 0.04 mg/m2/day KW-2189 appears to be the maximal  
tolerated dose, especially for patients who have received prior  
chemotherapy.

At this dose level, the drug was well tolerated, and the toxicities  
were  
acceptable.  
IT 154889-68-6, KW-2189  
RL: ADV (Adverse effect, including toxicity); BAC (Biological  
activity or

L14 ANSWER 30 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN

AN 1998:553501 CAPLUS

DN 129:289966

TI Efficient synthesis of the pharmacophore of the highly potent  
antitumor

antibiotic CC-1065

AU Tietze, Lutz F.; Buhr, Wilh; Looft, Jan; Grote, Thomas

CS Institut für Organische Chemie der Georg August-Universität Göttingen,  
Göttingen, D-37077, Germany

SO Chemistry—A European Journal (1998), 4(8), 1554-1560

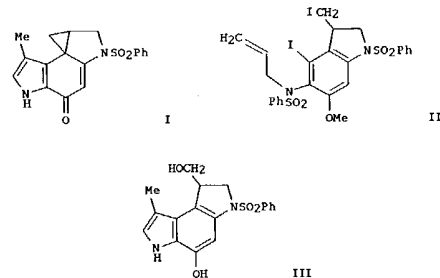
CODEN: CEUJED; ISSN: 0947-6539

PB Wiley-VCH Verlag GmbH

DT Journal

LA English

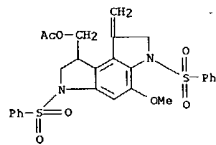
GI



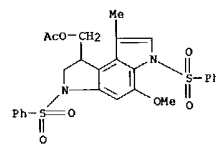
AB The pharmacophore CPI I of the potent antitumor antibiotic CC-1065 was  
synthesized in a very short reaction sequence of 11 steps with an  
overall  
yield of 23%. The key steps are two consecutive cyclizations  
mediated by  
organotransition metal complexes, which form first the pyrroline and  
then  
the pyrrole ring in I. Thus, halogen metal exchange of the  
N,N'-bisallylbromobenzene with Me3CLi and subsequent reaction with  
Cp2ZrMeCl gave II as a single product in 60% yield after quenching  
with  
two equivalent of iodine. Transformation of the iodomethyl group in  
II into  
an acetoxymethyl group, followed by Heck reaction, isomerization, and  
reductive cleavage, provided the pyrroloindoline system III, which was

10/069,202

L14 ANSWER 30 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 converted into I.  
 IT 165817-13-0P 165817-15-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT  
 (Reactant or reagent)  
 (efficient synthesis of pharmacophore of highly potent antitumor  
 antibiotic CC-1065)  
 RN 165817-13-0 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol,  
 1,2,3,6,7,8-hexahydro-5-methoxy-8-  
 methylene-3,6-bis(phenylsulfonyl)-, acetate (ester) (9CI) (CA INDEX  
 NAME)



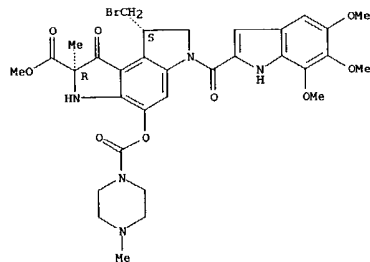
RN 165817-15-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol,  
 1,2,3,6-tetrahydro-5-methoxy-8-  
 methyl-3,6-bis(phenylsulfonyl)-, acetate (ester) (9CI) (CA INDEX  
 NAME)



RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 31 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 (Reactant or reagent)  
 (practical synthesis of high-quality antitumor agent KW-2189 from  
 duocarmycin B2 using a facile one-pot synthesis of intermediate)  
 RN 154901-65-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
 1,2,3,6,7,8-hexahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-1  
 -  
 oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,  
 (2R,8S)-  
 (9CI) (CA INDEX NAME)

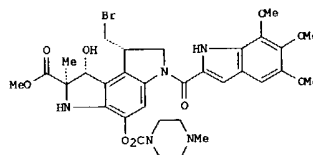
Absolute stereochemistry.



RN 160819-29-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
 1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-4-[[[4-methyl-1-  
 piperazinyl]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,  
 methyl ester, (1R,2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

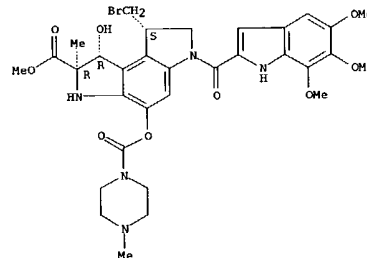
L14 ANSWER 31 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1998:536379 CAPLUS  
 DN 129:302469  
 TI Practical Synthesis of the High-Quality Antitumor Agent KW-2189 from  
 Duocarmycin B2 Using a Facile One-Pot Synthesis of an Intermediate  
 AU Kinugawa, Masahiko; Nagamura, Satoru; Sakaguchi, Akihiko; Masuda,  
 Yoshiaki; Saito, Hiromitsu; Ogasa, Takehiro; Kasai, Masaji  
 CS Sakai Research Laboratories, Kyowa Hakko Kogyo Co., Osaka, 590, Japan  
 SO Organic Process Research & Development (1998), 2(6), 344-350  
 CODEN: OPAPDF; ISSN: 1083-6160  
 PB American Chemical Society  
 UT Journal  
 LA English  
 GI



I

AB A facile and large-scale preparation process of a potent antitumor  
 agent  
 KW-2189, derived from the antitumor antibiotic duocarmycin B2, has  
 been developed. This new synthetic route required three steps: (i) one-pot  
 carbonylation and subsequent reduction, (ii) Wagner-Meerwein  
 rearrangement of the methoxycarbonyl group for the production of the pyrrole compound,  
 and (iii)  
 formation of the hydrobromide salt. The key strategic improvement  
 was to  
 obtain good quality hydroxy compound I in a reasonable yield without  
 isolation of the unstable keto intermediate. During com.-scale  
 production at  
 a scale of about 50 g, this strategy provided high-quality KW-2189 in  
 a  
 55% overall yield from duocarmycin B2. Potential degradation compds.  
 were  
 also synthesized and shown to be absent in the KW-2189 prepared  
 IT 154901-65-2P 160819-29-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT

L14 ANSWER 31 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



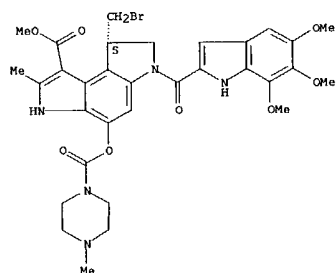
IT 154889-68-6P 160819-28-3P 171599-29-4P  
 214051-54-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (practical synthesis of high-quality antitumor agent KW-2189 from  
 duocarmycin B2 using a facile one-pot synthesis of intermediate)  
 RN 154889-68-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-  
 tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-[(5,6,7-  
 trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.



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L14 ANSWER 31 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

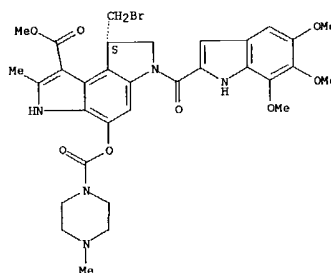


RN 160819-28-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 31 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

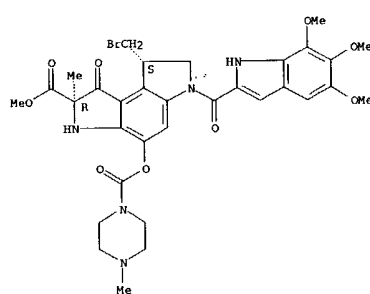
RN 171599-29-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HBr

L14 ANSWER 31 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



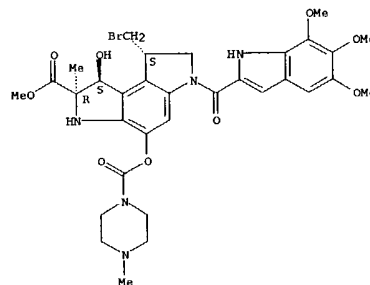
PAGE 2-A

● HCl

RN 214051-54-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1S,2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 31 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/069,202

L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STM (Continued)  
 AN 1998:527333 CAPLUS  
 DN 129:161451  
 TI Preparation of antitumor and antimicrobial pyrroloindole derivatives and their intermediates.  
 IN Fukuda, Yasumichi; Shimazawa, Rumiko; Omori, Yasuo; Terashima, Shiro  
 PA Kyocin Pharmaceutical Co., Ltd., Japan; Sagami Chemical Research Center  
 SO PCT Int. Appl., 32 pp.  
 CODEN: PIXX02  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9832757	A1	19980730	WO 1998-JP234	19980122
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 10265473	A2	19981006	JP 1998-7211	19980119
AU 9855760	A1	19980818	AU 1998-55760	19980122
EP 972775	A1	20000119	EP 1998-900695	19980122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI, TW 491846, US 6080859, JP 1997-11289, JP 1998-7211, WO 1998-JP234, MARPAT 129:161451	B, A, A, A, W	20020621, 20000627, 19970124, 19980119, 19980122	TW 1998-87101164, US 1999-341872	19980123, 19990719

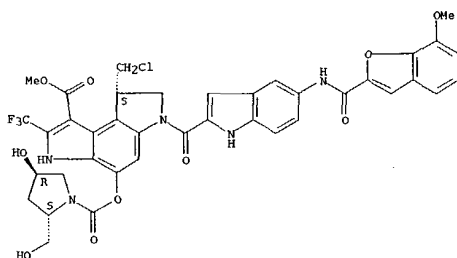
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The title compds. [I: R1 = OH, pyrrolidinyl; n = 1, 2; R2 = lower (C1-4) alkyl; Y-Y or Y-X = CH2, CHOH, CH2-CH2, O-CH2 or NMe-CH2; Z1 = Cl or Br; and Ar1 = Q-Q4; Z2, Z3 = O, NH; m = 1-4 integer; and Ar2 = Q-Q3 above] are prepared. Thus, I [R = H] was reacted with (2S)-pyrrolidine-2-methanol in

L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STM (Continued)

RN 211053-33-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[(2S,4R)-4-hydroxy-2-(hydroxymethyl)-1-pyrrolidinyl]carbonyl]oxy]-6-[[5-[[7-methoxy-2-benzofuranyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 211053-34-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[5-[[7-methoxy-2-benzofuranyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-4-[[[(2S)-2-(1-pyrrolidinylmethyl)-1-pyrrolidinyl]carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

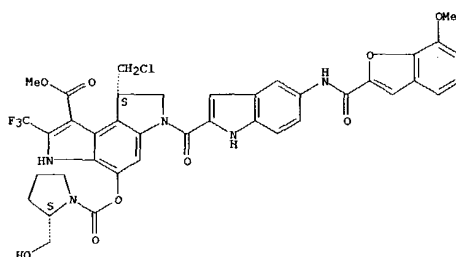
L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STM (Continued)  
 THF contg. 4-nitrophenyl chloroformate and Et3N to give II [R = (S)-2-(hydroxymethyl)pyrrolidin-1-ylcarbonyl]. In an in vitro study using female mice II [R = 2-(hydroxymethyl)piperidinocarbonyl] (also prep'd.) at 1.0 mg/Kg s.c. showed ca. 99% inhibition of the growth of adriamycin-resistant strain of M5076 cells. The stability of I was also studied.

IT 211053-32-6P 211053-33-7P 211053-34-8P  
 211053-35-9P 211053-36-0P 211053-37-1P  
 211053-38-2P 211053-39-3P 211053-40-6P  
 211053-41-7P 211053-42-8P

RI: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREF (Preparation); USES (Uses) (Preparation of antitumor and antimicrobial pyrroloindole derivs. and their intermediates)

RN 211053-32-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[(2S)-2-(hydroxymethyl)-1-pyrrolidinyl]carbonyl]oxy]-6-[[5-[[7-methoxy-2-benzofuranyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

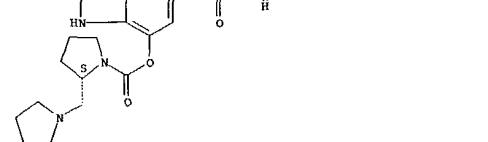
Absolute stereochemistry.



L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STM (Continued)

RN 211053-35-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[(2S)-2-(1-pyrrolidinylmethyl)-1-pyrrolidinyl]carbonyl]oxy]-6-[[5-[[7-methoxy-2-benzofuranyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



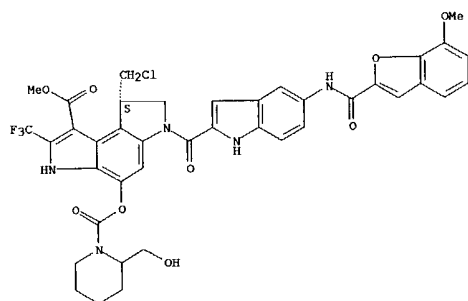
• HCl

RN 211053-35-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[(2S)-2-(1-pyrrolidinylmethyl)-1-pyrrolidinyl]carbonyl]oxy]-6-[[5-[[7-methoxy-2-benzofuranyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/069,202

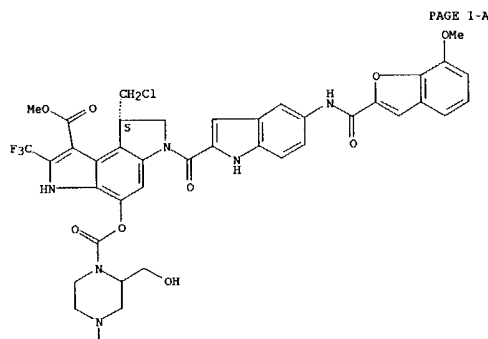
L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 211053-36-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-4-[[[2-(hydroxymethyl)-4-methyl-1-piperazinyl]carbonyl]oxy]-6-  
[[5-[[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-  
(trifluoromethyl)-, methyl ester, monohydrochloride, (8S)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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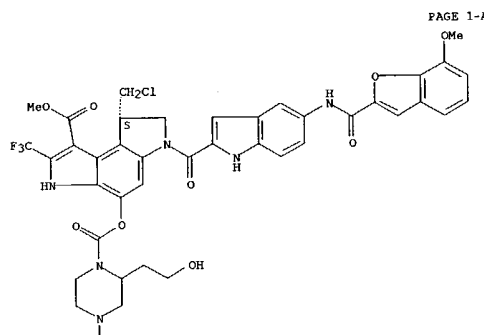
Me

● HCl

RN 211053-37-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-4-[[[2-(2-hydroxyethyl)-4-methyl-1-piperazinyl]carbonyl]oxy]-6-  
[[5-[[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-  
(trifluoromethyl)-, methyl ester, monohydrochloride, (8S)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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PAGE 2-A

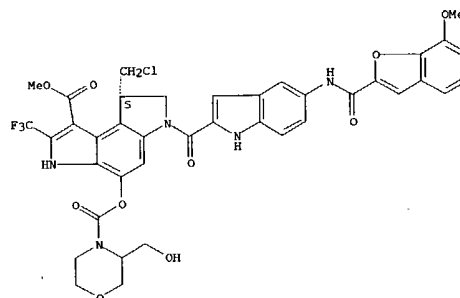
Me

● HCl

RN 211053-38-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-4-[[[3-(hydroxymethyl)-4-morpholinyl]carbonyl]oxy]-6-[[5-[[[(7-  
methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-  
(trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

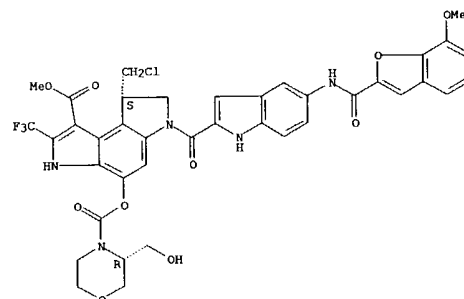
Absolute stereochemistry.

L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 211053-39-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-4-[[[3-(3-(hydroxymethyl)-4-morpholinyl)carbonyl]oxy]-6-[[5-  
[[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-  
(trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

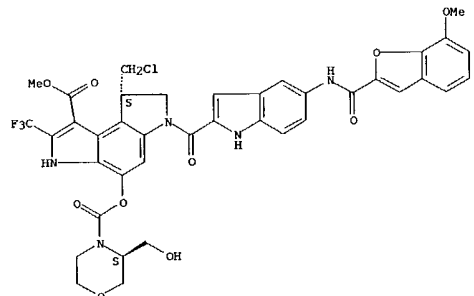


10/069,202

L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 211053-40-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-4-[[[(3S)-3-(hydroxymethyl)-4-morpholinyl]carbonyl]oxy]-6-[[5-  
[[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-  
(trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

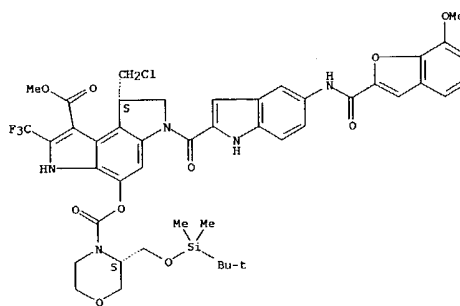
Absolute stereochemistry.



RN 211053-41-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[(13R)-  
3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-  
morpholinyl]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[[5-[[[(7-methoxy-2-  
benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-,  
methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

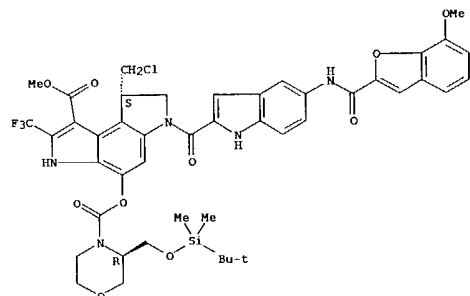
L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 211053-42-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[(13R)-  
3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-  
morpholinyl]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[[5-[[[(7-methoxy-2-  
benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-,  
methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



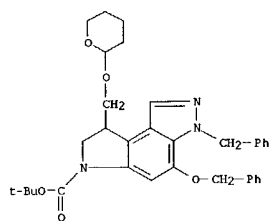
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 33 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

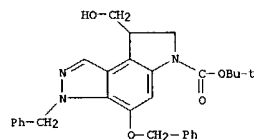
AN 1998:J29287 CAPLUS  
DN 129:67620  
TI Synthesis, solvolytic stability and cytotoxicity of a modified  
derivative  
of CPzI, a pyrazole analog of the alkylation subunit of the antitumor  
agent CC-1065: effect of the nitrogen substitution on the functional  
reactivity  
AU Baraldi, Pier Giovanni; Cacchiari, Barbara; Guiotto, Andrea; Romagnoli,  
Romeo; Spalluto, Giampiero; Zaid, Abdel Naser; Capolongo, Laura;  
Cozzi,  
Paolo; Geroni, Cristina; Mongelli, Nicola  
CS Dipartimento di Scienze Farmaceutiche, Universita di Ferrara, Ferrara,  
44100, Italy  
SO Farmaco (1997), 52(12), 717-723  
CODEN: FRMCE8; ISSN: 0014-827X  
PB Societa Chimica Italiana  
DT Journal  
LA English  
AB The synthesis and the comparative preliminary biol. evaluation of a  
new  
pyrazole analog, (±)-5-benzyl-2-(tert-butyloxycarbonyl)-1,2,8,8a-  
tetrahydrocyclopropa[c]pyrazo[4,3-e]indol-4-one (I), of the CC-1065  
alkylating unit (CPI) are described. I showed low cytotoxicity  
against  
L1210 murine leukemia (IC50 3064 nM) with respect to reference  
compound, but  
contrarily to literature data, was found to be more stable to  
solvolytic  
than the natural derivative (±)-N-Boc-CPI (pH 3, t1/2 = 212 h vs. 37  
h).  
The results of such investigation showed that alkylation of the  
pyrazole  
nitrogen caused a loss of cytotoxic activity in vitro against tumor  
cells.  
This exptl. observation allowed us to confirm the importance of free  
N-H  
for the anticellular activity.  
IT 209050-33-9P 209050-34-0P 209050-35-1P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT  
(Reactant or reagent)  
(synthesis and cytotoxicity of pyrazole analog of antitumor agent  
CC-1065)  
RN 209050-33-9 CAPLUS  
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 7,8-dihydro-4-  
(phenylmethoxy)-3-(phenylmethyl)-8-[[[(tetrahydro-2H-pyran-2-yl)oxy]methyl]-  
, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

10/069,202

L14 ANSWER 33 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 209050-34-0 CAPLUS  
 CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-3-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 209050-35-1 CAPLUS  
 CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-3-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 34 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:197505 CAPLUS

UN 128:243876

TI Intermediates for the preparation of duocarmycin SA and its derivatives

thereof, and process for the production of the intermediates

IN Fukuda, Yasumichi; Terashima, Shiro

PA Kyorin Pharmaceutical Co., Ltd., Japan; Sagami Chemical Research Center; ...

Fukuda, Yasumichi; Terashima, Shiro

SO PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

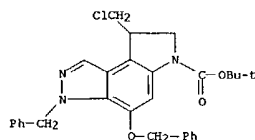
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9812197	A1	19980326	WO 1997-JP2207	19970626
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, SG, SI, SK, TR, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 10087666	A2	19980407	JP 1996-246097	19960918
AU 9732749	A1	19980414	AU 1997-32749	19970626
EP 937726	A1	19980825	EP 1997-928473	19970626
EP 937726	B1	20030312		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1230960	A	19991006	CN 1997-198004	19970626
CN 1090632	B	20020911		
AT 234304	E	20030315	AT 1997-928473	19970626
US 6066742	A	20000523	US 1999-254515	19990309
KR 2000036211	A	20000626	KR 1999-702272	19990317
PRAI JP 1996-246097	A	19960918		
WO 1997-JP2207	W	19970626		
OS CASREACT 128:243876; MARPAT 128:243876				
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Indole derivs. I [R1, R2, R3 = protecting group; R4 = C1-6 alkyl, benzyl] undergo oxidative cyclization to give title compds. II. Thus, indoline

III was reacted with Me-CHBr-COOMe in benzene containing 1,8-bis(dimethylamino)naphthalene to give 97% (3S)-I [R1 = BOC, R2 = acetyl].

L14 ANSWER 33 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 34 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

R3 = benzyl, R4 = Me], which was oxidized with MnO2 in N,N-dimethylacetamide contg. p-nitrobenzoic acid and palladium acetate to

give 23% the title compd. (-)-(S)-II [R1-R4 same as above].

IT 197657-12-8P 197657-13-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(preparation of intermediates for preparation of duocarmycin SA and its derivs.)

RN 197657-12-8 CAPLUS

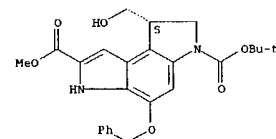
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,

7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-,

6-(1,1-dimethylethyl)

2-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



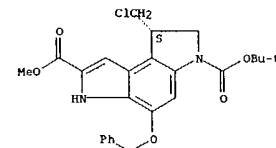
RN 197657-13-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,

8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)

2-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 197657-11-7P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of intermediates for preparation of duocarmycin SA and its derivs.)

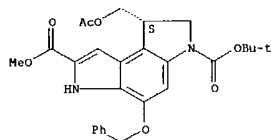
RN 197657-11-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,

10/069,202

L14 ANSWER 34 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (S)- (9CI) (CA INDEX NAME)

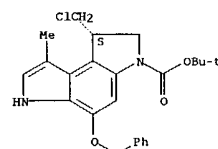
Absolute stereochemistry. Rotation (-).



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 35 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1998:191565 CAPLUS  
 DN 128:270457  
 TI Novel synthesis of optically active CC-1065, U-73,975 (adozelesin), U-80,244 (carzelesin), U-77,779 (bizelesin), KW-2189, and DU-86  
 AU Fukuda, Yasumichi; Furuta, Hirotsugu; Shiga, Futoshi; Asahina, Yoshikazu  
 CS Terasima, Shiro  
 CS Central Research Laboratories, Kyorin Pharmaceutical Co. Ltd.,  
 Tochigi,  
 329-01, Japan  
 SO Heterocycles (1997), 45(12), 2303-2308  
 CODEN: HETCYM; ISSN: 0365-5414  
 PB Japan Institute of Heterocyclic Chemistry  
 DT Journal  
 LA English  
 OS CASREACT 128:270457  
 AB The title syntheses were achieved by the method featuring oxidative cyclization of the enamino esters [(S)-13 and (S)-24] derived from the 5-aminoindoline [(S)-12], acylation with various structural types of indole-2-carboxylic acids, and formation of cyclopropylpyrroloindole moieties.  
 IT 110314-50-6P 112836-67-6P 156295-31-7P  
 156295-32-8P 156295-33-9P 176685-39-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT  
 (Reactant or reagent)  
 (synthesis of CC-1065, U-73,975 (adozelesin), U-80,244 (carzelesin),  
 U-77,779 (bizelesin), KW-2189, and DU-86)  
 RN 110314-50-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-  
 (9CI)  
 (CA INDEX NAME)

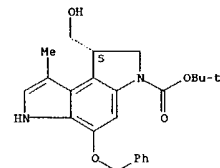
Absolute stereochemistry.



RN 112836-67-6 CAPLUS

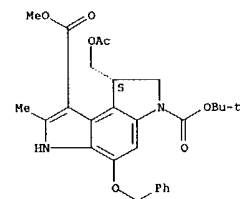
L14 ANSWER 35 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 156295-31-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
 8-[(acetyloxy)methyl]-7,8-dihydro-2-methyl-4-(phenylmethoxy)-,  
 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

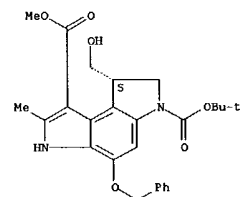
Absolute stereochemistry.



RN 156295-32-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
 7,8-dihydro-8-(hydroxymethyl)-2-methyl-4-(phenylmethoxy)-,  
 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

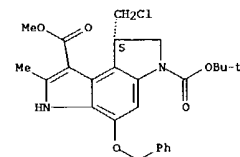
Absolute stereochemistry.

L14 ANSWER 35 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 156295-33-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
 8-(chloromethyl)-7,8-dihydro-2-methyl-4-(phenylmethoxy)-,  
 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

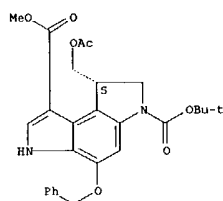


RN 176685-39-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

10/069,202

L14 ANSWER 35 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



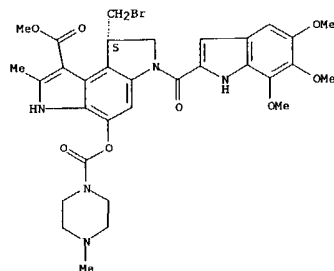
IT 154089-68-6P, KW-2189

RL: SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of CC-1065, U-73,975 (adozelesin), U-80,244(carzelesin),  
U-77,779 (bizelesin), KW-2189, and DU-86)RN 154089-68-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 35 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 36 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:180874 CAPLUS

DN 128:243950

TI Preparation of indolylcarbonylbenzindoles and analogs as antitumor

IN Denny, William Alexander; Tercel, Moana; Atwell, Graham John  
PA Auckland Division Cancer Society of New Zealand Inc., N. Z.; Denny,  
William Alexander; Tercel, Moana; Atwell, Graham John

SO PCT Int. Appl., 78 pp.

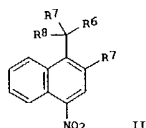
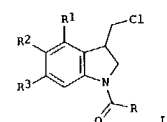
CODEN: PIKX02

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FI	WO 9811101	A2	19980319	WO 1997-N2117	19970912
	WO 9811101	A3	19980423		
DE,	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,				
	DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP,				
KR,	KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,				
NZ,	PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA,				
UG,	US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
FR,	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,				
GA,	GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,				
	GN, ML, MR, NE, SN, TD, TG				
	AU 9744039	A1	19980402	AU 1997-44039	19970912
	AU 721037	B2	20000622		
	EP 938474	A2	19990901	EP 1997-942316	19970912
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,				
PT,	IE, FI				
	NZ 334344	A	20000825	NZ 1997-334344	19970912
	JP 2000517292	T2	20001226	JP 1997-537492	19970912
	US 6130237	A	20001010	US 1999-266966	19990312
PRAI	GB 1996-19082	A	19960912		
	GB 1997-7394	A	19970410		
	WO 1997-N2117	W	19970912		
OS	MARPAT 128:243950				
GI					



L14 ANSWER 36 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

AB Title compds. [I: R = heterocycl(ethenyl); R1R2 = CH:CHCH:CH,  
CH:CR5NH,  
etc.; R3 = NO2, NH2, NHOH, SH, alkylthio, etc.; R4 = halo, OSO2H,  
alkylsulfonyloxy, etc.; R5 = CO2H, alkoxycarbonyl, etc.] were  
prepared for  
use in, e.g., ADEPT therapy. Thus, naphthylmalonate II (R6 = H, R7 =  
CON3, R7 = R8 = CO2Me) (preparation given) was cyclized to give I (R6R7 = CONH,  
R7 = R8 = CO2Me) which was converted in 5 steps to II (R6R7 =  
CH2NCO2OMe3,  
R7 = CH2Cl, R8 = H). The latter was deprotected and the product  
N-acylated by 5,6,7-trimethoxyindole-2-carboxylic acid to give I (R =  
5,6,7-trimethoxyindol-2-yl, R1R2 = CH:CHCH:CH, R3 = NO2, R4 = Cl).Data  
for biol. activity of I were given.

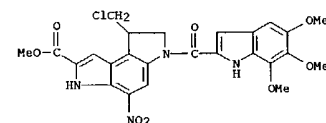
IT 204915-56-OP 204915-58-2P 204915-59-3P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological  
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic  
use);BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of indolylcarbonylbenzindoles and analogs as antitumor  
prodrugs)

RN 204915-56-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,

8-(chloromethyl)-3,6,7,8-  
tetrahydro-4-nitro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,  
methyl  
ester (9CI) (CA INDEX NAME)

RN 204915-58-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
4-amino-8-(chloromethyl)-  
6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,  
methyl  
ester, compd. with ethyl acetate (2:1) (9CI) (CA INDEX NAME)

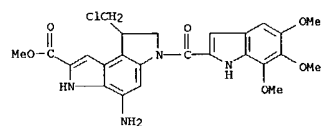
CH 1

CRN 204915-57-1

CMF C25 H25 Cl N4 O6

10/069,202

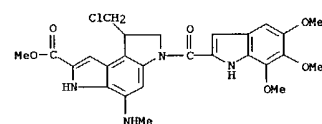
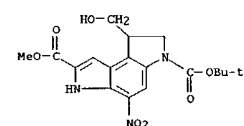
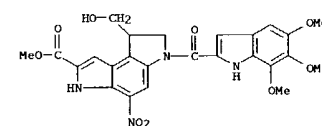
L14 ANSWER 36 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



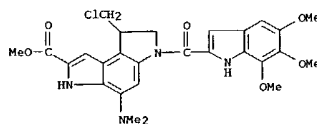
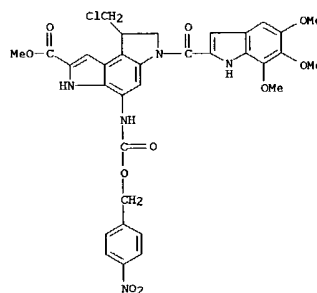
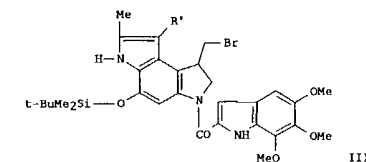
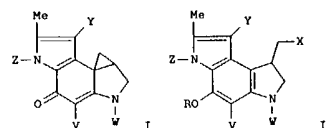
CM 2

CRN 141-78-6  
CMF C4 H8 O2

Et-O-Ac

RN 204915-59-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-tetrahydro-4-(methylamino)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,  
methyl ester (9CI) (CA INDEX NAME)RN 204915-60-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-4-(dimethylamino)-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)L14 ANSWER 36 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
ester (9CI) (CA INDEX NAME)RN 204916-11-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-4-nitro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,  
methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 36 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

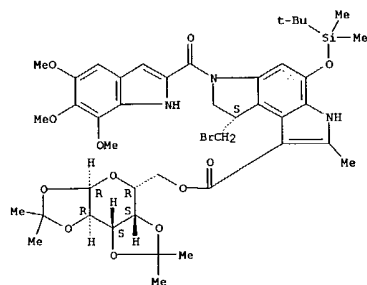
RN 204915-61-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[(4-nitrophenyl)methoxycarbonyl]amino]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)IT 204916-10-9P 204916-11-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RAC (Reactant or reagent)  
(preparation of indolylcarbonylbenzindoles and analogs as antitumor prodrugs)  
RN 204916-10-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,  
7,8-dihydro-8-(hydroxymethyl)-4-nitro-, 6-[(1,1-dimethylethyl) 2-methylL14 ANSWER 37 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1998:175925 CAPLUS  
DN 128:243875  
TI Preparation of antitumor DC-89 derivatives  
IN Amishiro, Nobuyoshi; Saito, Hiromitsu; Okamoto, Akihiko; Okabe, Masami  
PA Kyowa Hakko Kogyo Co., Ltd., Japan; Amishiro, Nobuyoshi; Saito, Hiromitsu; Okamoto, Akihiko; Okabe, Masami  
SO PCT Int. Appl., 100 pp.  
CODEN: PIXXD2  
DT Patent  
LA Japanese  
FAN: CNT 1  
PATENT NO. KIND DATE APPLICATION NO. DATE  
PI WO 9809966 A1 19980312 WO 1997-JP3089 19970903  
W: AU, BG, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RO, SG,  
SI, SK, UA, US, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
PT, SE AU 9741345 A1 19980326 AU 1997-41345 19970903  
PRAI JP 1996-232723 19960903  
WO 1997-JP3089 19970903  
OS MARPAT 128:243875  
GI

AB DC-89 derivs. I and II [Y = H, halo, (un)substituted alkyl, COR1, OR2, SR3, etc.; R1 = H, (un)substituted alkyl, (un)substituted aralkyl, etc.;

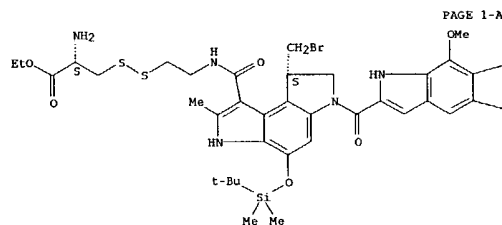


L14 ANSWER 37 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)  
 R2 = H, (un)substituted alkyl, (un)substituted alkenyl,  
 (un)substituted  
 aryl, etc.; R3 = H, (un)substituted alkyl, (un)substituted alkenyl,  
 (un)substituted aryl, (un)substituted heterocyclyl; W = H, acyl such  
 as  
 substituted acryloyl, etc.; Z = H, (un)substituted alkyl,  
 (un)substituted  
 alkenyl, (un)substituted aryl, COR9, etc.; R9 = H, acyl, silyl; V =  
 H,  
 halo, NO2, etc.; X = Cl, Br; R = H, OH, alkoxy, aryl, etc.] and their  
 pharmaceutically acceptable salts are prepd. E.g., the title compd.  
 III  
 [R' = Me] was prepd. in 56% yield by reduct. of III [R' = COOMe] with  
 DIBAL-H in THF. In an in vitro study, II [Y = CH2NMe2, R = V = Z =  
 H, X =  
 Cl, W = 5,6,7-trimethoxy-1H-indol-2-ylcarbonyl] HCl (also prepd.)  
 had an  
 IC50 of 0.28 nM against HeLa53 tumor cells.  
 IT  
 205050-82-4P 205050-84-6P 205050-96-0P  
 205051-05-4P 205051-09-8P 205051-11-2P  
 205051-13-4P  
 R1: BAC (Biological activity or effector, except adverse); BSU  
 (Biological  
 study, unclassified); RCT (Reactant); SPN (Synthetic preparation);  
 THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT  
 (Reactant or reagent); USES (Uses)  
 (preparation of antitumor DC-89 derivs.)  
 RN 205050-82-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-4-[[[(1,1-  
 dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-  
 trimethoxy-1H-indol-2-yl)carbonyl]-, phenyl ester, (S)- (9CI) (CA  
 INDEX  
 NAME)  
 Absolute stereochemistry.

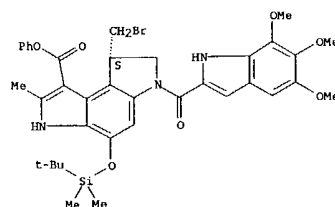
L14 ANSWER 37 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)  
 Absolute stereochemistry.



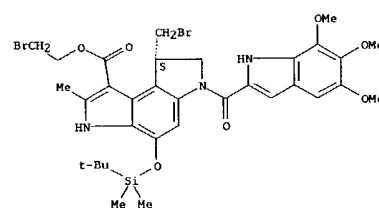
RN 205051-05-4 CAPLUS  
 CN L-Alanine, 3-[[[2-[[[(8S)-8-(bromomethyl)-4-[[[(1,1-  
 dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-  
 trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrole-1-  
 yl]carbonyl]amino]ethyl]dithio]-, ethyl ester (9CI) (CA INDEX NAME)  
 Absolute stereochemistry.



L14 ANSWER 37 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)



RN 205050-84-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-4-[[[(1,1-  
 dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-  
 trimethoxy-1H-indol-2-yl)carbonyl]-, 2-bromoethyl ester, (8S)- (9CI)  
 (CA  
 INDEX NAME)  
 Absolute stereochemistry.



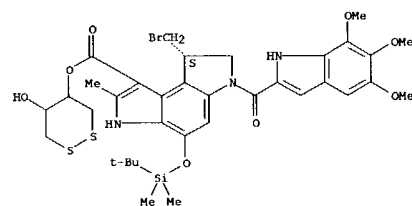
RN 205050-96-0 CAPLUS  
 CN α-D-Galactopyranose, 1,2:3,4-bis-O-(1-methylethylidene)-,  
 (8S)-8-(bromomethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-  
 tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-  
 b:4,3-b']dipyrrole-1-carboxylate (9CI) (CA INDEX NAME)

L14 ANSWER 37 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)

PAGE 1-B



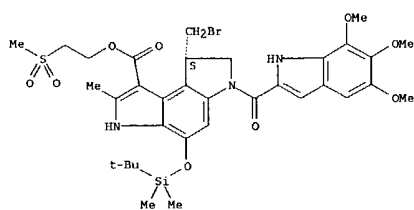
RN 205051-09-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-4-[[[(1,1-  
 dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-  
 trimethoxy-1H-indol-2-yl)carbonyl]-, 5-hydroxy-1,2-dithian-4-yl ester,  
 (8S)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry.



RN 205051-11-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-4-[[[(1,1-  
 dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-  
 trimethoxy-1H-indol-2-yl)carbonyl]-, 2-(methylsulfonyl)ethyl ester,  
 (8S)-  
 (9CI) (CA INDEX NAME)  
 Absolute stereochemistry.

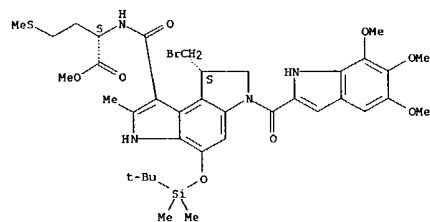
10/069,202

L14 ANSWER 37 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 205051-13-4 CAPLUS  
CN L-Methionine, N-[[[(8S)-8-(bromomethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrole-1-yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

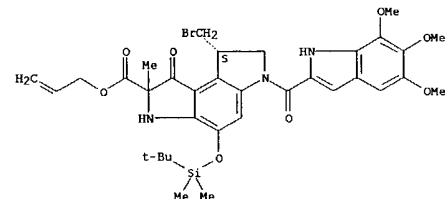
Absolute stereochemistry.



IT 129953-15-7 177958-19-9 205051-55-4  
205051-56-5 205051-57-6  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of antitumor DC-89 derivs.)  
RN 129953-15-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester, (8S)- (9CI) (CA INDEX NAME)

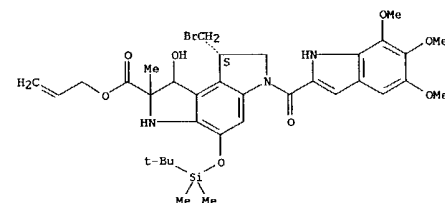
L14 ANSWER 37 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 205051-56-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester, (8S)-[partial]- (9CI) (CA INDEX NAME)

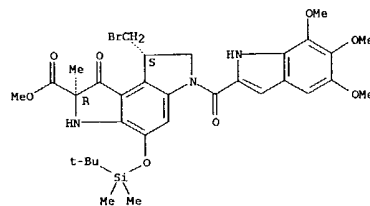
Absolute stereochemistry.



RN 205051-57-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester, (8S)- (9CI) (CA INDEX NAME)

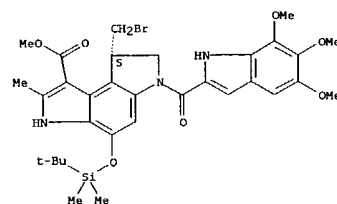
L14 ANSWER 37 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 177958-19-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

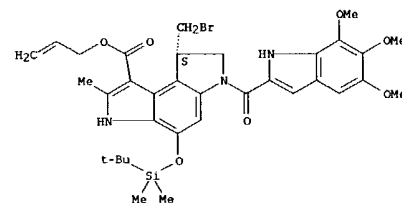
Absolute stereochemistry.



RN 205051-55-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester, (8S)- (9CI) (CA INDEX NAME)

L14 ANSWER 37 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
INDEX NAME)

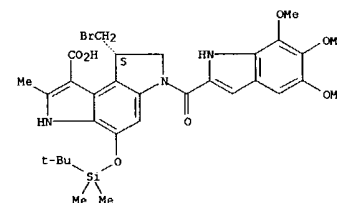
Absolute stereochemistry.



IT 205051-58-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT (Reactant or reagent)  
(preparation of antitumor DC-89 derivs.)

RN 205051-58-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

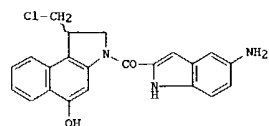
10/069,202

L14 ANSWER 38 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AN 1997:791611 CAPLUS  
 DN 128:110513  
 TI In vitro enhancement of antitumor activity of a water-soluble  
 duocarmycin  
 derivative, KW-2189, by caffeine-mediated DNA-repair inhibition in  
 human  
 lung cancer cells  
 AU Ogasawara, Hayato; Nishio, Kazuto; Ishida, Tomoyuki; Arioka, Hitoshi;  
 Fukuoka, Kazuya; Saijo, Nagahiro  
 CS Pharmacology Division, National Cancer Center Research Institute,  
 Tokyo,  
 104, Japan  
 SO Japanese Journal of Cancer Research (1997), 88(11), 1033-1037  
 CODEN: JJCREF; ISSN: 0910-5050  
 PB Japanese Cancer Association  
 DT Journal  
 LA English  
 AB Duocarmycins, including KW-2189, bind in the minor groove of  
 double-stranded DNA at A-T-rich sequences, followed by covalent  
 bonding  
 with N-3 of adenine in preferred sequences. We examined the effect  
 of  
 DNA-repair modulators, such as caffeine and aphidicolin, on the  
 cytotoxicity of duocarmycins towards human lung cancer cells, as  
 determined by  
 dye formation assay. Caffeine (0.5 or 1 mM), but not aphidicolin,  
 enhanced the growth-inhibitory activity of KW-2189, DU-86, and  
 duocarmycin  
 5A. Caffeine inhibited repair of DNA strand breaks induced by  
 KW-2189, as  
 assayed by the alkaline elution technique. This suggests that  
 duocarmycin-induced DNA strand breaks, which are potentially lethal  
 to  
 cells, are repaired through a caffeine-sensitive pathway.  
 IT 154889-68-6, KW-2189  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological  
 study, unclassified); THU (Therapeutic use); BIOL (Biological  
 study); USES  
 (Uses)  
 (in vitro enhancement of antitumor activity of a water-soluble  
 duocarmycin  
 derivative, KW-2189, by caffeine-mediated DNA-repair inhibition  
 in human  
 lung cancer cells)  
 RN 154889-68-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-  
 tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-  
 trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (85)- (9CI) (CA  
 INDEX

L14 ANSWER 39 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AN 1997:783786 CAPLUS  
 DN 128:48468  
 TI Preparation of DNA-binding glucuronide indoles immuno-conjugates as  
 antitumors  
 IN Wang, Yunqiang; Wright, Susan C.; Larrick, James W.  
 PA Panorama Research, Inc., USA  
 SO PCT Int. Appl., 79 pp.  
 CODEN: PIXX02  
 DT Patent  
 LA English  
 FAN.CNT 1  

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9744000	A2	19971127	WO 1997-US9055	19970522
WO 9744000	A3	19971231		

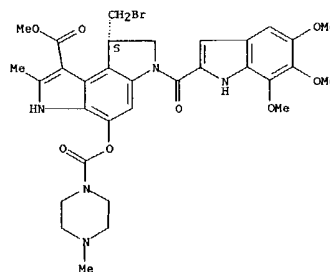
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,  
 DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR,  
 KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,  
 PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ,  
 VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR,  
 GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,  
 GN, ML, MR, NE, SN, TD, TG  
 US 5843937 A 19981201 US 1996-652883 19960523  
 AU 9732170 A1 19971209 AU 1997-32170 19970522  
 EP 918752 A2 19990602 EP 1997-927798 19970522  
 R: AT, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE  
 CN 1219841 A 19990616 CN 1997-194862 19970522  
 JP 2000511893 T2 20000912 JP 1997-542898 19970522  
 PRAI US 1996-652883 A 19960523  
 WO 1997-US9055 W 19970522  
 OS MARPAT 128:48468  
 GI



AB The present invention relates to novel DNA alkylating agents and the  
 prodrugs of these agents which are useful as antitumors and DNA  
 labeling

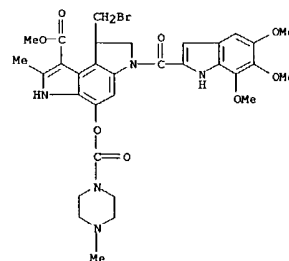
L14 ANSWER 38 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)  
 NAME)

Absolute stereochemistry.



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 39 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)  
 agents. The compds. are hydroxydihydrobenzindole oligopeptides and  
 prodrugs thereof wherein the monomeric constituents are derived from  
 monocyclic, or bicyclic heterocyclic arom. residues. Thus, indole 1  
 was  
 prepd. and tested for its antitumor activity with cytotoxicity (IC50 =  
 0.09 nM).  
 IT 134106-78-8P  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological  
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic  
 use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of DNA-binding glucuronide hydroxydihydrobenzindole  
 oligopeptides immuno-conjugates as antitumors)  
 RN 134106-78-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-  
 tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-  
 trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX  
 NAME)



10/069,202

L14 ANSWER 40 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:716591 CAPLUS

DN 128:57126

TI Synthesis, cytotoxicity, antitumor activity and sequence selective binding

of two pyrazole analogs structurally related to the antitumor agents U-71,184 and adozelesin

AU Baraldi, Pier Giovanni; Cacciari, Barbara; Romagnoli, Romeo; Spalluto,

Giampiero; Gambari, Roberto; Bianchi, Nicoletta; Passadore, Marco; Ambrosino, Piera; Mongelli, Nicola; Cozzi, Paolo; Geroni, Cristina

CS Dipartimento di Scienze Farmaceutiche, Ferrara, I-44100, Italy

SO Anti-Cancer Drug Design (1997), 12(7), 555-576

CODEN: ACUDEA; ISSN: 0266-9536

PB Oxford University Press

DT Journal

LA English

AB Two pyrazole analogs structurally related to the antitumor agents adozelesin and U-71,184 resp. were synthesized. By using a

polymerase chain reaction approach, both compds. show selective binding to A +

T rich

sequences exactly as reference compound U-71,184. In in vitro

assays, against

L1210 cell lines, both derivs. showed cytotoxicity in the  $\mu$ M range,

values

comparable with the natural target compound (+)-CC-1065. The most active

compound showed very high antitumor activity in mice implanted with

L1210

cells (ILS<sub>1</sub> 363).

IT 187034-23-7P 187034-24-8P 187034-25-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(preparation and antitumor activity and DNA binding of pyrazole analogs

related to U-71,184 and adozelesin)

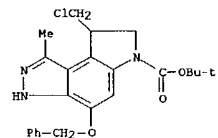
RN 187034-23-7 CAPLUS

CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 7,8-dihydro-1-methyl-4-

(phenylmethoxy)-3-(tetrahydro-2H-pyran-2-yl)-8-[[[tetrahydro-2H-pyran-2-yl)oxy]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 40 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

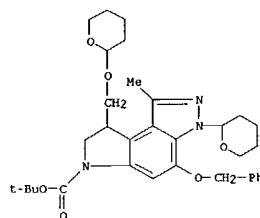
(Continued)



RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 40 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

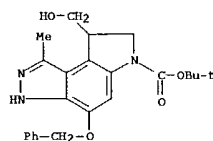
(Continued)



RN 187034-24-8 CAPLUS

CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-1-methyl-4-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI)

(CA INDEX NAME)



RN 187034-25-9 CAPLUS

CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 8-(chloromethyl)-7,8-dihydro-1-methyl-4-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 41 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:707375 CAPLUS

DN 127:318803

TI A novel synthesis of (+)-duocarmycin SA

AU Fukuda, Yasumichi; Terashima, Shiro

CS Central Research Laboratories, Kyorin Pharmaceutical Co. Ltd., Nogi, 329-01, Japan

SO Tetrahedron Letters (1997), 38(41), 7207-7208

CODEN: TELEAY; ISSN: 0040-4039

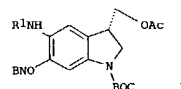
PB Elsevier

DT Journal

LA English

OS CASREACT 127:318803

GI



AB The title synthesis was achieved in eight steps from

(S)-5-aminoindoline

(I) (R1 = H) by a method featuring sequential dehydrogenation, double

bond isomerization, and oxidative cyclization of (S)-5-[(1-methoxycarbonyl)ethyl]aminoindoline (II) [I, R1 = (S)-CH(Me)CO2Me] as

the

key steps. The sequential reaction was effected by using MnO2-Pd(OAc)2 as

the oxidizing agent in the presence of an acid catalyst.

IT 197657-11-7P 197657-12-8P 197657-13-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(synthesis of (+)-duocarmycin SA)

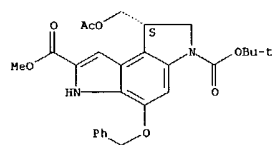
RN 197657-11-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-[(1,1-dimethylethyl) 2-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

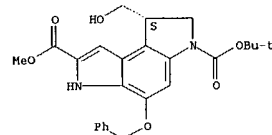
10/069,202

L14 ANSWER 41 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 197657-12-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,  
7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-,  
6-(1,1-dimethylethyl)  
2-methyl ester, (S)- (9CI) (CA INDEX NAME)

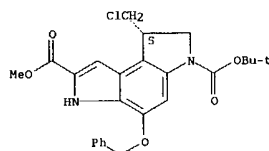
Absolute stereochemistry. Rotation (-).



RN 197657-13-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,  
8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-,  
6-(1,1-dimethylethyl)  
2-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L14 ANSWER 41 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 42 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:468982 CAPLUS

DN 127:185373

TI Synthesis and antitumor activity of novel cyclopropapyrroloindole  
(CPI)

derivatives bearing methoxycarbonyl and trifluoromethyl groups

AU Fukuda, Yasumichi; Furuta, Hirotsugu; Shiga, Futoshi; Oomori, Yasuo;  
Kusama, Yoshie; Ebisu, Hiroyuki; Terashima, Shiro  
CS Central Research Laboratories, Kyorin Pharmaceutical Co. Ltd., Nogi,  
329-01, Japan

SO Bioorganic & Medicinal Chemistry Letters (1997), 7(13), 1683-1688

CODEN: BMCLEB; ISSN: 0960-894X

PB Elsevier

DT Journal

LA English

AB The title synthesis was achieved by employing oxidative cyclization  
of the

enamino ester as a key step. Some of these novel

3-methoxycarbonyl-2-

trifluoromethylcyclopropapyrroloindole (MCTFCPI) derivs. were found

to

exhibit antitumor activity against murine leukemia and murine solid

tumors

more prominent than that of known CPI derivs.

IT 194361-61-OP

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic

use);

BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis and antitumor activity of cyclopropapyrroloindole

derivs. bearing methoxycarbonyl and trifluoromethyl groups)

RN 194361-61-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,

8-(bromomethyl)-3,6,7,8-

tetrahydro-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-2-(trifluoromethyl)-6

-

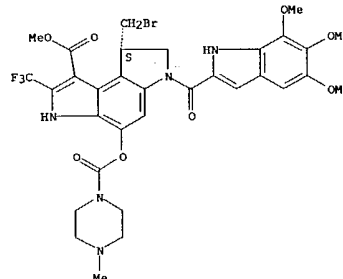
[[[5,6,7-trimethoxy-1H-indol-2-yl]carbonyl]-, methyl ester,

monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L14 ANSWER 42 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



● HCl

PAGE 2-A

IT 154889-68-6, KW 2189

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study);

USES

(Uses)

(synthesis and antitumor activity of cyclopropapyrroloindole

derivs. bearing methoxycarbonyl and trifluoromethyl groups)

RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,

8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-[[[5,6,7-

trimethoxy-1H-indol-2-yl]carbonyl]-, methyl ester, (8S)- (9CI) (CA

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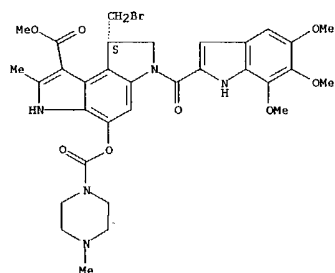
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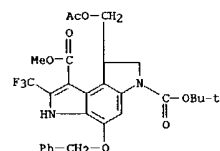
NAME)

10/069,202

L14 ANSWER 42 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 194093-62-4P 194093-63-5P 194093-64-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (synthesis and antitumor activity of cyclopropapyrroloindole  
 deriva.  
 bearing methoxycarbonyl and trifluoromethyl groups)  
 RN 194093-62-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-,  
 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)

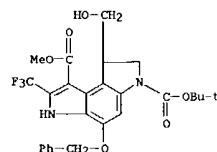


RN 194093-63-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-2-(trifluoromethyl)-,

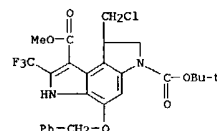
L14 ANSWER 43 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:436161 CAPLUS  
 DN 127:130933  
 TI Sequence and Structure Dependence of the Hybridization-Triggered  
 Reaction  
 of Oligonucleotides Bearing Conjugated Cyclopropapyrroloindole  
 AU Lukhtanov, Eugeny A.; Kutyavin, Igor V.; Gorn, Vladimir V.; Reed,  
 Michael  
 W.; Adams, A. David; Lucas, Deborah D.; Meyer, Rich B., Jr.  
 CS Epoch Pharmaceuticals Inc., Bothell, WA, 98021, USA  
 SO Journal of the American Chemical Society (1997), 119(27), 6214-6225  
 CODEN: JACSAT; ISSN: 0002-7863  
 PB American Chemical Society  
 UT Journal  
 LA English  
 AB Oligodeoxyribonucleotides (ODNs) with conjugated reactive groups are  
 potential sequence-specific gene inactivating agents. The antitumor  
 antibiotic CC-1065 binds preferably in the minor groove of A-T-rich  
 sites  
 of double-stranded DNA, and the cyclopropapyrroloindole (CPI)  
 subunit of  
 the drug alkylates adenines at their N3 position. Pure enantiomeric  
 (+)-  
 and (-)-CPI and its N5-Me homolog (MCPI) were synthesized and  
 conjugated  
 to an ODN. These conjugates were evaluated for their ability to  
 alkylate  
 a target containing a duplex region immediately adjacent to a  
 single-stranded  
 complementary binding region for the ODN conjugate. The conjugates  
 demonstrated excellent stability in physiol. conditions and  
 stereospecific, hybridization-triggered alkylation of the synthetic  
 ODN  
 targets. The dependence of the reaction rates on sequence of the  
 duplex  
 target region was in accord with the predicted minor groove binding  
 of the  
 conjugated CPI. The reactivity was highly dependent on the  
 structure of  
 the crosslinking group. Natural (+)-enantiomers alkylate 10-20 times  
 faster than the corresponding (-)-enantiomers. Regiospecificity of  
 the  
 alkylation reaction is conferred by the length of the spacer arm.  
 N5-Methylation of the CPI moiety suppresses the reactivity by a  
 factor of  
 3-5. Addition of a  
 1,2-dihydro-3H-pyrrolo[3,2-e]indole-7-carboxylate (DPI)  
 binding subunit of CC-1065 between CPI or MCPI residues and an ODN  
 results  
 in a significant enhancement of the reactivity which is especially  
 pronounced  
 for (-)-enantiomers. The main products of sequence-specific  
 alkylation  
 were determined for complexes with the most efficient reactions.  
 IT 192657-43-5P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (cyclopropapyrroloindole-conjugated oligonucleotide preparation  
 and target

L14 ANSWER 42 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



RN 194093-64-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-,  
 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)

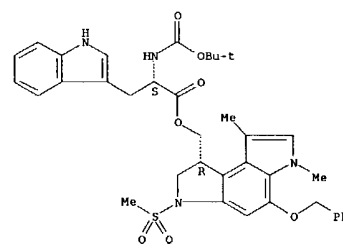


RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 43 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 hybridization-assocd. alkylation)

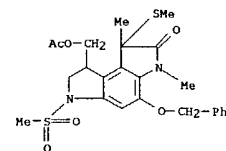
RN 192657-43-5 CAPLUS  
 CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-,  
 [(1R)-1,2,3,6-tetrahydro-  
 6,8-dimethyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-  
 b']dipyrrol-1-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 192657-40-2P 192657-42-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT (Reactant or reagent)  
 (preparation and reaction; cyclopropapyrroloindole-conjugated  
 oligonucleotide preparation and target hybridization-associated  
 alkylation)  
 RN 192657-40-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrol-2(1H)-one, 8-[(acetyloxy)methyl]-3,6,7,8-  
 tetrahydro-1,3-dimethyl-6-(methylsulfonyl)-1-(methylthio)-4-  
 (phenylmethoxy)- (9CI) (CA INDEX NAME)

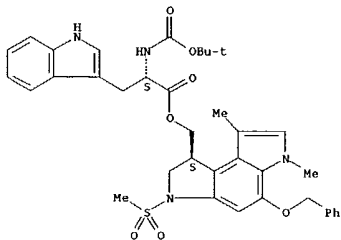


RN 192657-42-4 CAPLUS  
 CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-,  
 [(1S)-1,2,3,6-tetrahydro-

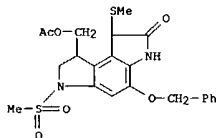
10/069,202

L14 ANSWER 43 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
6,8-dimethyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl)methyl ester (9CI) (CA INDEX NAME)

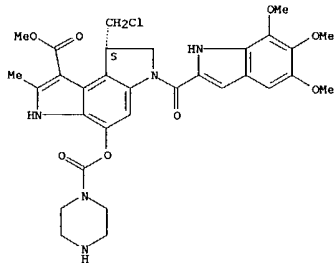
Absolute stereochemistry.



IT 112089-53-9  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction: cyclopropylpyrrolindole-conjugated oligonucleotide preparation and target hybridization-associated alkylation)  
RN 112089-53-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrol-2(1H)-one, 8-[(acetyloxy)methyl]-3,6,7,8-tetrahydro-6-(methylsulfonyl)-1-(methylthio)-4-(phenylmethoxy)-(9CI) (CA INDEX NAME)



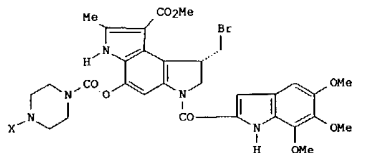
L14 ANSWER 44 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 192509-07-2P 192509-08-3P 192509-09-4P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of [3H]KW-2189)  
RN 192509-07-2 CAPLUS  
CN 1,4-Piperazinedicarboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-(methoxycarbonyl)-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl 1,1-dimethylethyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 44 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1997:404887 CAPLUS  
DN 127:108790  
TI The synthesis of [3H]KW-2189, a novel active antitumor antibiotic  
AU Nagamura, Satoru; Kinugawa, Masahiko; Ogasa, Takehiko; Saito, Hiromitsu  
CS Kyowa Hakko Kogyo Co. Ltd., Tokyo Research Laboratories, Machida, 194, Japan  
SO Journal of Labelled Compounds & Radiopharmaceuticals (1997), 39(6), 471-477  
CODEN: JLCRD4; ISSN: 0362-4803  
PB Wiley  
DT Journal  
LA English  
GI



AB The synthesis of [3H]KW-2189 (I, X = C3H3), a novel active antitumor antibiotic, is described. The key intermediate I (X = H) in the synthesis, was synthesized in four steps from duocarmycin B2.

Treatment of I (X = H) with [3H]methyl iodide in the presence of NaHCO3 in MeOH-Me2CO (1:1) afforded the [3H]KW-2189 with highly specific activity of 86.4 Ci/mmol.

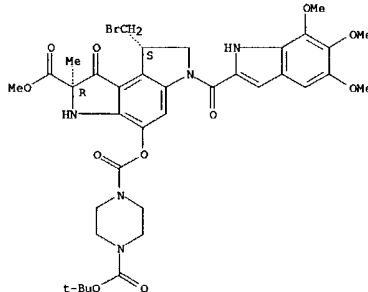
IT 192509-08-1P  
RL: BYP (Byproduct); PREP (Preparation)  
(preparation of [3H]KW-2189)

RN 192509-06-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[(1-piperazinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

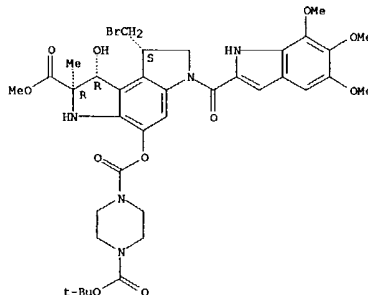
Absolute stereochemistry.

L14 ANSWER 44 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 192509-08-3 CAPLUS  
CN 1,4-Piperazinedicarboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1-hydroxy-2-(methoxycarbonyl)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl 1,1-dimethylethyl ester, (1R-[1a,2P,8a])- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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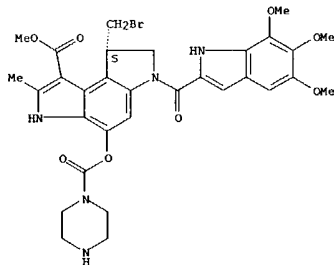
L14 ANSWER 44 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 192509-09-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[(1-piperazinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 192509-10-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of [3H]KW-2189)

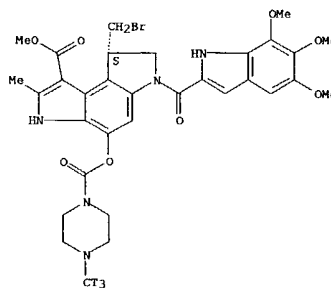
RN 192509-10-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[4-(methyl-t3)-1-piperazinylcarbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 44 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 45 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT 190060-22-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

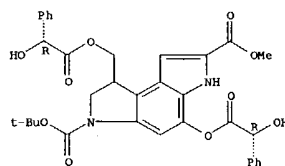
RACT (Reactant or reagent)  
(duocarmycin SA shortened, simplified, and extended agents: a systematic examination of the role of the DNA binding subunit)

RN 190060-22-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,

7,8-dihydro-4-[(hydroxyphenylacetyl)oxy]-8-[[[(hydroxyphenylacetyl)oxy]methyl]-, 6-(1,1-dimethylethyl) 2-methyl ester, [4(R),8(R)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 45 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:324291 CAPLUS

DN 127:12962

TI Duocarmycin SA shortened, simplified, and extended agents: a systematic

examination of the role of the DNA binding subunit

AU Boger, Dale L.; Hertzog, Donald L.; Bollinger, Bernd; Johnson, Douglas S.;

Cai, Hui; Goldberg, Joel; Turnbull, Philip

CS Department of Chemistry, Scripps Research Institute, La Jolla, CA, 92037,

USA

SO Journal of the American Chemical Society (1997), 119(21), 4977-4986

CODEN: JACSAT; ISSN: 0002-7863

PB American Chemical Society

DT Journal

LA English

AB The examination of shortened, simplified, and extended analogs of duocarmycin

SA are described and constitute a detailed study of the role of linked DNA binding subunit. In addition to enhancing the DNA binding affinity and

selectivity through minor groove noncovalent contacts, the studies in conjunction with those of the accompanying article illustrate that an extended rigid N2 amide substituent is required for catalysis of the

DNA alkylation reaction. This activation for DNA alkylation is independent of pH, and we propose it results from a binding-induced conformational change

in the agents which increases their inherent reactivity. The ground state destabilization of the substrate results from a twist in the linking amide

that disrupts the vinylogous amide stabilization of the alkylation subunit

and activates the agent for nucleophilic addition. This leads to preferential

activation of the agents for DNA alkylation within the narrower, deeper

AT-rich minor groove sites where the inherent twist in the linking amide

and helical rise of the bound conformation is greatest. Thus, shape-selective recognition (preferential AT-rich noncovalent

binding) and shape-dependent catalysis (induced twist in linking N2 amide)

combine to restrict SN2 alkylation to accessible adenine N3 nucleophilic sites

within the preferred binding sites. Adnl. ramifications of this DNA binding-induced conformational change on the reversibility of the DNA

alkylation reaction are discussed. The results of the study illustrate

the importance of the C5' methoxy group and the C6 Me ester of duocarmycin

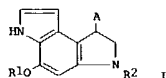
SA, and a previously unrecognized role for these substituents is proposed.



10/069,202

L14 ANSWER 46 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1997:262265 CAPLUS  
 DN 126:277505  
 TI Preparation of 8-methylpyrroloindole derivatives as antibiotics and antitumor agents  
 IN Fukuda, Yasuji; Furuta, Kosuke; Terajima, Atsuro  
 PA Kyorin Seiyaku KK, Japan; Sagami Chem Res  
 SO Jpn. Kokai Tokkyo Koho, 3 pp.  
 CODEN: JKKXAF  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 09067374	A2	19970311	JP 1995-223056	19950831
PRAI	JP 1995-223056		19950831		
OS	MAPAT 126:277505				
GI					

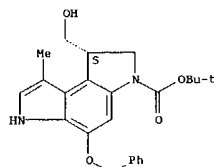


AB The title compds. [1; Y = Me; R1 = protecting group of amino; A = CH2X1;  
 OR5; R2;  
 R5 = protecting group of OH] are prepared by reduction of I (Y = CO2R3; R3 = linear or branched C1-6 alkyl; A = CH2X2; X2 = halo, OH, OSO2R4, etc.; R1, R2 = same as above). I, useful as antibiotics and antitumor agents (no data) or intermediates thereof, are prepared efficiently and easily.  
 Thus, I (Y = CO2Me, A = CH2OAc, R1 = tert-butoxycarbonyl, R2 = C6H4CH2) was refluxed with BH3.THF in THF for 19 h and treated with aqueous citric acid to give the title compound I (Y = Me, A = CH2OH, R1, R2 = same as above).  
 IT 112836-67-6P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of 8-methylpyrroloindole derivs. as antibiotics and antitumor)

L14 ANSWER 46 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

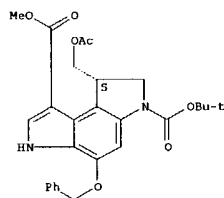
L14 ANSWER 46 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 agents)  
 RN 112836-67-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester,  
 (S)-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



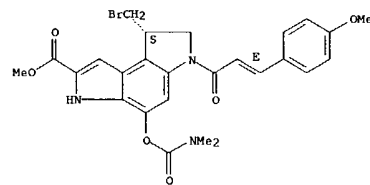
IT 176695-39-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of 8-methylpyrroloindole derivs. as antibiotics and antitumor agents)  
 RN 176695-39-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L14 ANSWER 47 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1997:228843 CAPLUS  
 DN 126:311725  
 TI Studies on duocarmycin SA and its derivatives  
 AU Nagamura, Satoru; Asai, Akira; Kobayashi, Eiji; Gomi, Katsushige; Saito, Hiromitsu  
 CS Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd, Machida, 194, Japan  
 SO Bioorganic & Medicinal Chemistry (1997), 5(3), 623-630  
 CODEN: BMCECP; ISSN: 0968-0896  
 FB Elsevier  
 DT Journal  
 LA English  
 AB New duocarmycin SA derivs. have been synthesized and evaluated for in vitro anticellular activity against HeLa S3 cells, and in vivo antitumor activity against murine sarcoma 180 in mice. The results suggested that the N,N-dialkylcarbamoyl derivs. bearing the p-methoxy cinnamoyl group, prepared from duocarmycin SA, showed good in vivo antitumor activities superior to native duocarmycin SA.  
 IT 152718-07-5P 152718-08-6P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation);  
 BIOL (Biological study); PREP (Preparation)  
 (antitumor activity, preparation, and structure of duocarmycin SA derivs.)  
 RN 152718-07-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-, methyl ester, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.

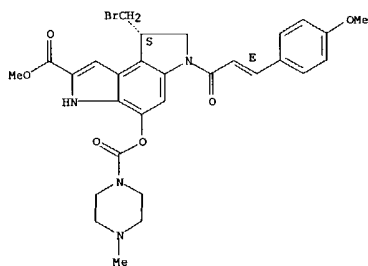


RN 152718-08-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

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L14 ANSWER 47 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



IT 152718-02-0P 152718-03-1P 152718-04-2P

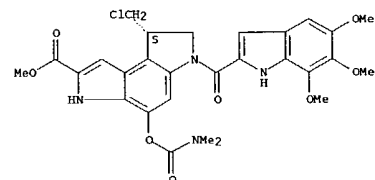
152718-05-3P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (antitumor activity, preparation, and structure of duocarmycin SA deriva.)

RN 152718-02-0 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

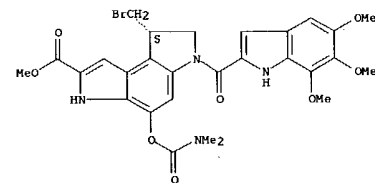
L14 ANSWER 47 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 RN 152718-04-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-4-[[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

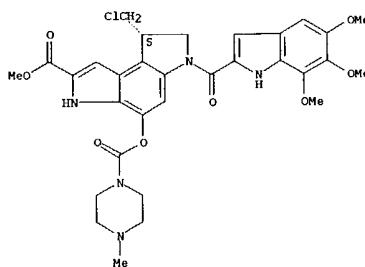


RN 152718-05-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



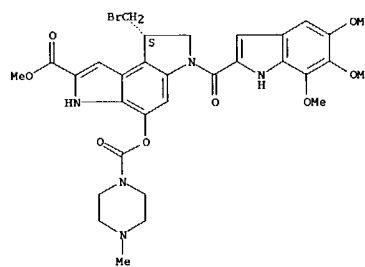
L14 ANSWER 47 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



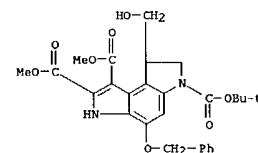
RN 152718-03-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



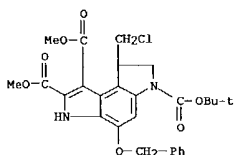
L14 ANSWER 48 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 RN 1997:219845 CAPLUS  
 DN 126:287689  
 TI Synthesis and antitumor activity of novel cyclopropapyrroleindole (CPI) derivatives bearing bis(methoxycarbonyl) groups  
 AU Fukuda, Yasumichi; Omori, Yasuo; Kusama, Yoshie; Terashima, Shiro  
 CS Central Research Laboratories, Kyorin Pharmaceutical Co. Ltd., Nogai, 329-01, Japan  
 SO Bioorganic & Medicinal Chemistry Letters (1997), 7(6), 749-752  
 CODEN: BMCLEB; ISSN: 0960-894X  
 FB Elsevier  
 DT Journal  
 LA English  
 AB The title synthesis was achieved by employing oxidative cyclization of the enaminodiester prepared by Michael addition of the 5-aminoindoline with di-Me acetylenedicarboxylate, as a key step. Some of these novel bis(methoxycarbonyl)cyclopropapyrroleindole (MC2CPI) derivs. 9c, d and their seco-chlorides 18c, d were found to exhibit prominent cytotoxicity and antitumor activity against P388 murine leukemia.  
 IT 156905-82-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and chlorination of)  
 RN 156905-82-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1,2-dimethyl ester (9CI) (CA INDEX NAME)



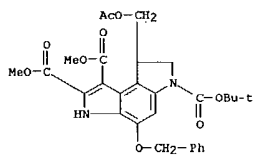
IT 156905-83-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and debenzoylation of)  
 RN 156905-83-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1,2-dimethyl ester (9CI) (CA INDEX NAME)

10/069,202

L14 ANSWER 48 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



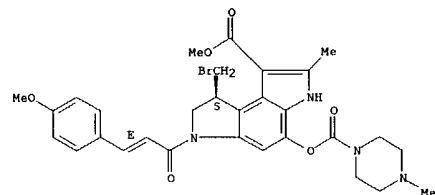
IT 156905-81-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (preparation and methanolysis of)  
 RN 156905-81-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid,  
 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1,2-dimethyl ester (9CI) (CA INDEX NAME)



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

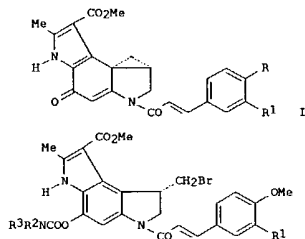
L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 contributed to an enhancement of water sol. Most of the  
 8-O-carbamoyl  
 derivs. II [R1 = H, R3R2N = 4-methylpyrazinyl,  
 4-piperidinopiperidinyl,  
 4-(isopropylaminocarbonylmethyl)piperazinyl; R1 = NMe2, NMe2,  
 3-aminopropoxy, NH2, OCH2CO2H, R3R2N = 4-methylpyrazinyl] of the  
 4'-methoxycinnamoyl derivs. displayed remarkably superior in vivo  
 antitumor activity to duocarmycin A or B2. It was noteworthy that  
 these  
 8-O-carbamoyl derivs. exhibited significant antitumor activity at a  
 wider  
 range of doses as compared with the A-ring pyrrole derivs. having the  
 trimethoxyindole skeleton in segment B.  
 IT 186760-19-0P 186760-20-3P  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological  
 study, unclassified); RCT (Reactant); SPN (Synthetic preparation);  
 BIOL  
 (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
 (synthesis and antitumor activity of DU-86, duocarmycin related,  
 derivs. with A-ring pyrrole compds. bearing cinnamoyl groups)  
 RN 186760-19-0 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-  
 tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-  
 methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA  
 INDEX  
 NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



RN 186760-20-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 6-[3-[3-(3-aminopropoxy)-4-  
 methoxyphenyl]-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-  
 methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester,  
 [S-(R)]-

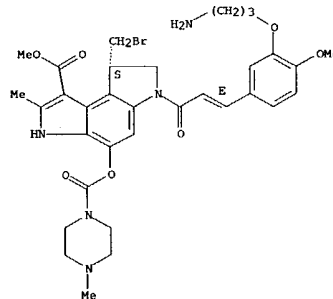
L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1997:180818 CAPLUS  
 DN 126:157310  
 TI Synthesis and Antitumor Activity of Duocarmycin Derivatives: A-Ring  
 Pyrrole Compounds Bearing Cinnamoyl Groups  
 AU Nagamura, Satoru; Asai, Akira; Amishiro, Nobuyoshi; Kobayashi, Eiji;  
 Gomi,  
 Kataushiger, Saito, Hiromitsu  
 C5 Tokyo Research Laboratories, Kyowa Hakko Kogyo Co. Ltd., Machida, 194,  
 Japan  
 SO Journal of Medicinal Chemistry (1997), 40(6), 972-979  
 CODEN: JMCMAR; ISSN: 0022-2623  
 FB American Chemical Society  
 DT Journal  
 LA English  
 GI



AB A series of DU-86 A segment N6-cinnamoyl derivs I (R = OMe,  
 n-propyloxy,  
 allyloxy, pentyloxy, 4-methoxybenzyloxy, OH, NMe2, NMe2, Me, Et,  
 NHCO2Me3, NH2, R1 = H; R = OMe, R1 = 3-azidopropoxy,  
 3-dimethylaminopropoxy, OCH2CO2Me3, OCH2CO2Me, NMe2, NMe2,  
 NHCO2Me3,  
 NH2, 3-aminopropoxy) were synthesized and evaluated for in vitro  
 anticellular activity against HeLa S3 cells and in vivo antitumor  
 activity  
 against murine sarcoma 180 in mice. The 4'-methoxy- and  
 4'-BocNH-cinnamoyl derivs. exhibited strong in vitro anticellular  
 activity  
 compared to the other synthesized compds. The substitution of the  
 4'-methoxycinnamoyl derivative did not affect the anticellular  
 activity and

L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.

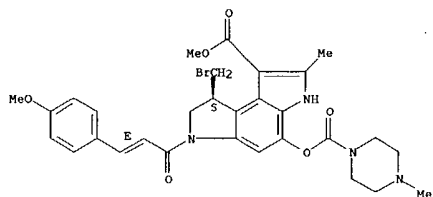


IT 186760-06-5P 186760-07-6P 186760-08-7P  
 186760-09-8P 186760-10-1P 186760-11-2P  
 186760-12-3P 186760-21-4P  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological  
 study, unclassified); SPN (Synthetic preparation); BIOL (Biological  
 study); PREP (Preparation)  
 (synthesis and antitumor activity of DU-86, duocarmycin related,  
 derivs. with A-ring pyrrole compds. bearing cinnamoyl groups)  
 RN 186760-06-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-  
 tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-  
 methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride,  
 (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.

10/069,202

L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



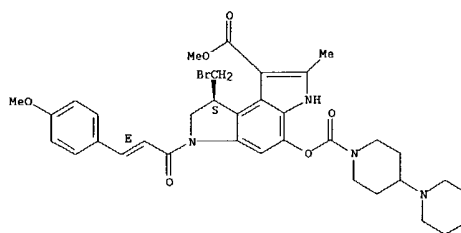
● HCl

RN 186760-07-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
4-[[[1,4'-bipiperidin]-1'-

ylcarbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-  
1-oxo-2-propenyl]-2-methyl-, methyl ester, monohydrochloride,  
[S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



● HCl

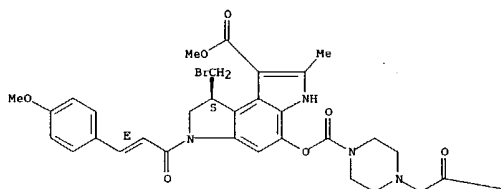
RN 186760-08-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[4-[2-[(1-  
methylethyl)amino]-2-oxoethyl]-1-piperazinyl]carbonyl]oxy]-, methyl  
ester, monohydrochloride, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

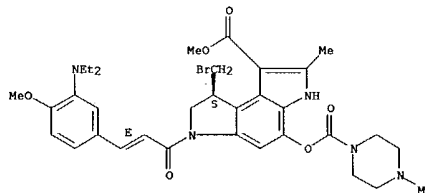
PAGE 1-A



● HCl

PAGE 1-B

L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



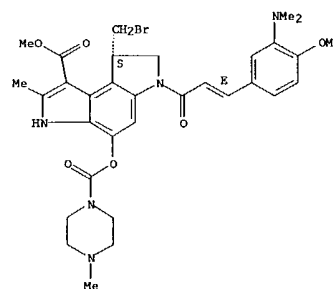
● 2 HCl

RN 186760-10-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-6-[3-[3-

(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-  
methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester,  
monohydrochloride, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

PAGE 1-A



—NHPr-i

RN 186760-09-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-6-[3-[3-

(diethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-  
methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester,  
dihydrochloride, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

10/069,202

L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A

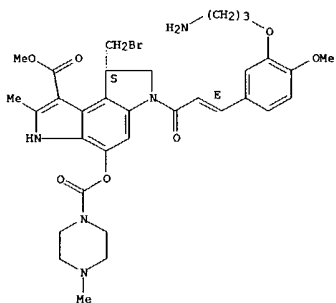
● HCl

RN 186760-11-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
6-[3-[3-(3-aminopropoxy)-4-

methoxyphenyl]-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-  
methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester,  
dihydrochloride, [5-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

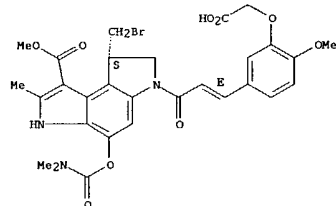
PAGE 1-A



● 2 HCl

PAGE 2-A

L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



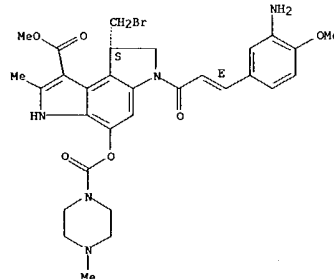
L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 186760-12-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-(3-amino-4-  
methoxyphenyl)-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-  
methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester,  
dihydrochloride, [5-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

PAGE 1-A



PAGE 2-A

● 2 HCl

RN 186760-21-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-6-[3-[3-  
(carboxymethyl)-4-methoxyphenyl]-1-oxo-2-propenyl]-4-  
[[[4-methyl-1-piperazinyl]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, 1-methyl  
ester, [8aS-[2(E),7bS\*,8aR\*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

L14 ANSWER 50 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:172312 CAPLUS

DN 126:171589

TI Preparation of pyrrolo[3,2-c]indazoles and analogs as antitumor agents

IN Cozzi, Faolo Baraldi, Pier Giovanni Beria, Italo Capolongo, Laura  
Spalluto, Giampiero

PA Pharmacia Spa, Italy

SO Brit. UK Pat. Appl., 64 pp.

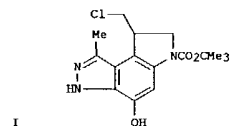
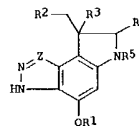
CODEN: BAXXDU

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 2300857	A1	19961120	GB 1995-10169	19950519
GB	2300857	B2	19980708		
PRAI	GB 1995-10169		19950519		
OS	MARPAT 126:171589				
GI					



AB Title compds. [e.g., I; R1 = H, alkyl, alkanoyl, alkylcarbamoyl,  
etc.; R2

= halos; R3,R4 = H or alkyl; R5 = H, COR7, (aryl)hydrocarbyl, etc.; R7

= (aryl)hydrocarbyl, alkoxy, etc.; Z = N or CR; R = H or alkyl] were

prepared

as antitumor agents (no data). Thus, 4-formyl-3-methylpyrazole

(preparation

given) was converted in 15 steps to title compound II.

IT 187033-75-6P 187033-76-7P

RU: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic

use);

BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrrolo[3,2-c]indazoles and analogs as antitumor

agents)

RN 187033-75-6 CAPLUS

CN Pyrrolo[3,2-c]indazole-6(3H)-carboxylic acid,

8-(chloromethyl)-7,8-dihydro-

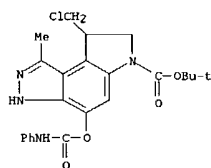
1-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, 1,1-dimethylethyl ester

(9CI)

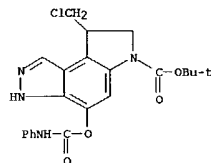
(CA INDEX NAME)

10/069,202

L14 ANSWER 50 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

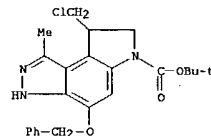


RN 187033-76-7 CAPLUS  
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid,  
8-(chloromethyl)-7,8-dihydro-  
4-[[ (phenylamino)carbonyl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA  
INDEX NAME)

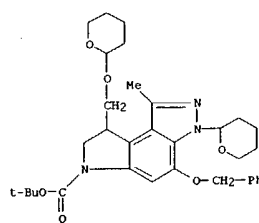


IT 187034-23-7P 187034-24-8P 187034-25-9P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT (Reactant or reagent)  
(preparation of pyrrolo[3,2-c]indazoles and analogs as antitumor  
agents)  
RN 187034-23-7 CAPLUS  
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 7,8-dihydro-1-methyl-4-  
(phenylmethoxy)-3-(tetrahydro-2H-pyran-2-yl)-8-[[ (tetrahydro-2H-pyran-2-  
yl)oxy]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

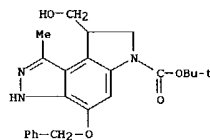
L14 ANSWER 50 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 50 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 187034-24-8 CAPLUS  
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 7,8-dihydro-8-  
(hydroxymethyl)-1-methyl-4-(phenylmethoxy)-, 1,1-dimethylethyl ester  
(9CI) (CA INDEX NAME)



RN 187034-25-9 CAPLUS  
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid,  
8-(chloromethyl)-7,8-dihydro-  
1-methyl-4-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX  
NAME)

L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:596991 CAPLUS

DN 125:328342

TI Synthesis and antitumor activity of duocarmycin derivatives:  
modification of segment A of duocarmycin B2

AU Nagamura, Satoru; Arai, Akira; Kanda, Yutaka; Kobayashi, Eiji; Gomi,  
Katsushige; Saito, Hiromitsu  
CS Tokyo Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Tokyo, 194, Japan  
SO Chemical & Pharmaceutical Bulletin (1996), 44(9), 1723-1730

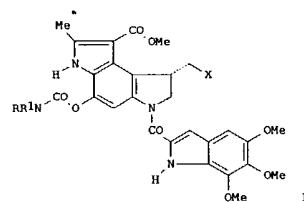
CODEN: CPBTAL; ISSN: 0009-2363

PB Pharmaceutical Society of Japan

DT Journal

LA English

GI



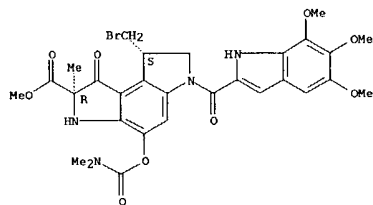
AB Several A-ring pyrrole derivs. of duocarmycin B2, e.g. I (RR1N = Me2N,  
4-Me-piperazinyl, piperidinyl, pyrrolidinyl, X = Br, Cl), were  
synthesized from the 3-hydroxy compds. by utilizing an interesting acid-catalyzed  
rearrangement, their anticellular activity was preliminarily  
evaluated by assays of growth inhibition of HeLa S3 cells (in vitro) and antitumor  
activity against murine sarcoma 180 (in vivo). The 8-O-N,N-  
dialkylcarbamoyl derivs. of the A-ring pyrrole compound showed  
remarkably potent in vivo antitumor activity, superior to that of duocarmycin B2.  
These derivs. were subjected to further biol. evaluation. They  
exhibited potent antitumor activity toward murine solid tumors including M5076  
sarcoma, B-16 melanoma and Colon 26 adenocarcinoma. Their most  
noteworthy feature was their efficacy against various human xenografts including  
LC-6 (lung), St-4 (stomach), and Co-3 (colon).  
IT 171599-25-0 171599-29-4  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); BIOL (Biological study)  
(synthesis and antitumor activity of duocarmycin derivs.)

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L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 RN 171599-25-0 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-

[[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-  
 [(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,  
 (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

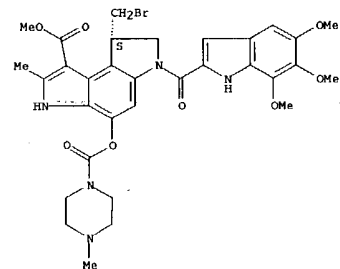


RN 171599-29-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-

1,2,3,6,7,8-hexahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-  
 oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,  
 monohydrochloride, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

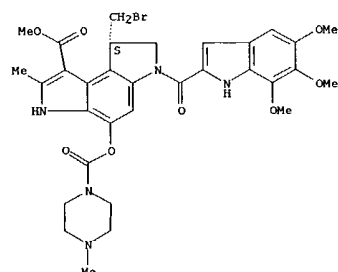
L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 160819-28-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-  
 trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide,  
 (8S)- (9CI) (CA INDEX NAME)

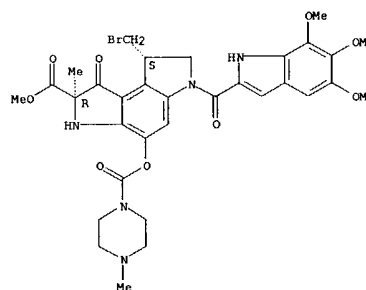
Absolute stereochemistry.



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L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



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● HCl

IT 154889-68-6P 160819-28-3P 177958-19-9P  
 177958-20-2P

RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation);  
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
 (synthesis and antitumor activity of duocarmycin derivs.)

RN 154889-68-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-  
 trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

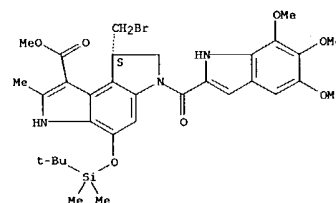
PAGE 2-A

● HBr

RN 177958-19-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-4-[[[(1,1-

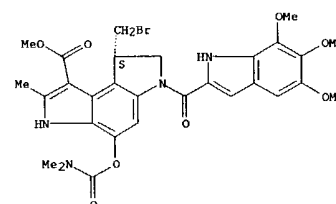
dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-  
 trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.



RN 177958-20-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-  
 [[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-  
 trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.



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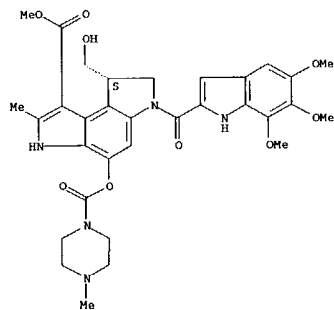
L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT 154715-68-1P 183240-24-6P 183240-25-7P  
183240-26-8P 183240-27-9P 183240-28-0P

RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(synthesis and antitumor activity of duocarmycin derivs.)

RN 154715-68-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



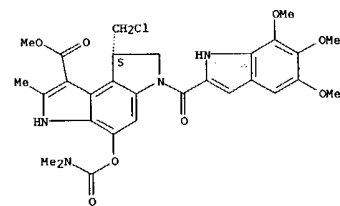
RN 183240-24-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[(1-piperidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

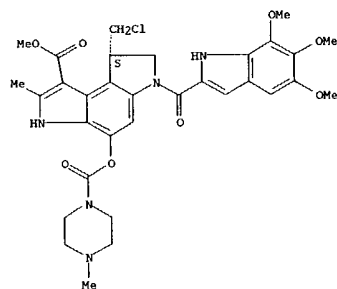
Absolute stereochemistry.



RN 183240-27-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

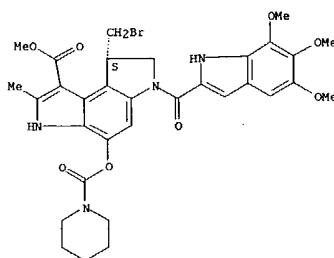
tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



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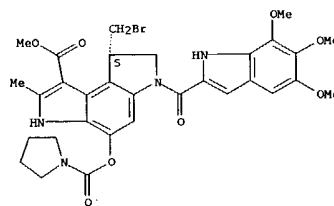
L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 183240-25-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[(1-pyrrolidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 183240-26-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

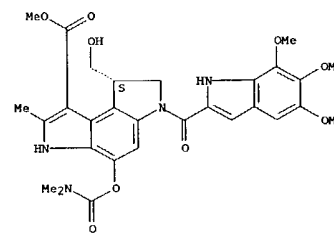
L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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● HCl

RN 183240-28-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 129953-15-7P 129953-17-9P 183240-30-4P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT (Reactant or reagent)  
(synthesis and antitumor activity of duocarmycin derivs.)

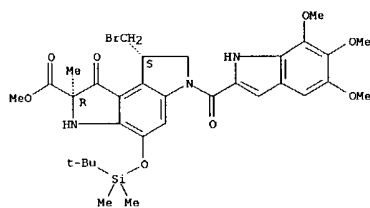
RN 129953-15-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



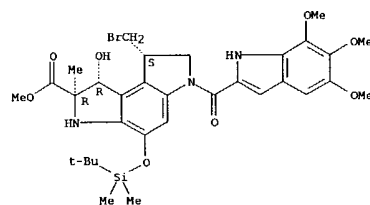
10/069,202

L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



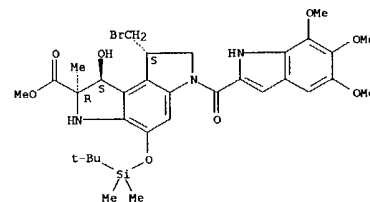
RN 129953-17-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-  
dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-  
6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,  
(1R,2R,8S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



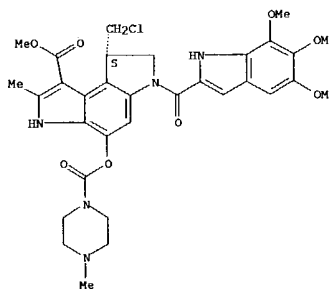
RN 183240-30-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA  
INDEX NAME)

L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

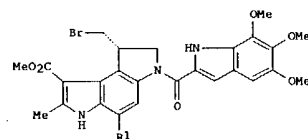
Absolute stereochemistry.



IT 183388-25-2P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(synthesis and antitumor activity of duocarmycin derivs.)  
RN 183388-25-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-  
dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-  
6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,  
(1R,2S,8S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1996:572393 CAPLUS  
DN 125:300656  
TI Synthesis and antitumor activity of duocarmycin derivatives: A-ring  
pyrrole analogs of duocarmycin B2  
AU Nagamura, Satoru; Kobayashi, Eiji; Gomi, Katsuhisa; Saito, Hiromitsu  
CS Tokyo Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Machida, 194, Japan  
SO Bioorganic & Medicinal Chemistry (1996), 4(8), 1379-1391  
CODEN: BMCECP; ISSN: 0968-0896  
PB Elsevier  
DT Journal  
LA English  
GI



AB A series of the eight-substituted A-ring pyrrole derivs. of  
duocarmycin B2  
I [ R = H, Me; R1 = PhCH2O, MeO, Me2N(CH2)2O, MeSO2O, F3CSO2O, H, NC,  
AcO,  
HCl.MeN(CH2)2N(CH2)2CO(CH2)3CO2, MeO2CO, PhO2CO, PhCH2O2CCH2NHCO2,  
HO2CCH2NHCO2, L-Phe-O, PhNHCO2, 4-MeOC6H4NHCO2,  
HCl.Me2CCHNHCO2CH2N(CH2)2N(CH2)2CO2, HCl.(CH2)5N(CH2)5NCO2,  
HO2CCH2N(Me)CO2,  
MeN(CH2)2N(CH2)2CO2] were synthesized, and evaluated for in vitro  
anticellular activity against HeLa S3 cells and in vivo antitumor  
activity  
against murine sarcoma 180 in mice. In addition, the stability of the  
analogs in aqueous solution was examined I (R = H, R1 = H, NC) which  
cannot  
structurally release the cyclopropane compound (DU-86), exhibited  
extremely  
diminished anticellular activity compared with duocarmycin A or DU-86.  
The ethers and the sulfonates which were not converted to DU-86 under  
usual conditions (35°C, pH 7), showed almost equal in vivo  
activities to that of duocarmycin A. However, their optimal doses  
were  
significantly higher than that for duocarmycin A. Most of the A-ring  
pyrrole analogs which can be chemical or enzymically converted to  
DU-86,  
displayed remarkably superior in vivo antitumor activity to  
duocarmycin A.  
These results suggest that the a-ring pyrrole analogs need to  
chemical or  
enzymically release DU-86 as an active metabolite to exhibit potent in

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L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

vivo antitumor activity.

IT 182360-43-6P 182360-56-1P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation);

BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and antitumor activity of A-ring pyrrole analogs of

duocarmycin B2)

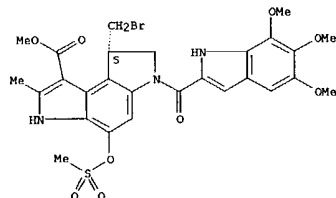
RN 182360-43-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,

8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[(methylsulfonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 182360-56-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,

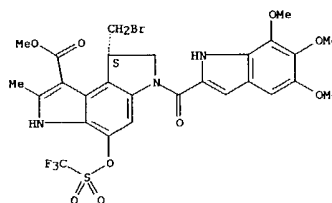
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[(trifluoromethyl)sulfonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 168776-83-8P 182360-42-5P 182360-48-1P

182360-49-2P 182360-50-3P 182360-52-7P

182360-55-0P 182360-60-7P 182360-61-8P

182360-63-0P 182360-65-2P 182360-66-3P

182360-67-4P 182360-68-5P 182578-89-8P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological

study); PREP (Preparation)

(synthesis and antitumor activity of A-ring pyrrole analogs of

duocarmycin B2)

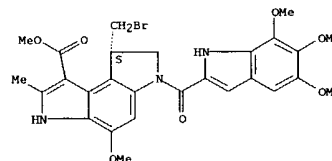
RN 168776-83-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,

8-(bromomethyl)-3,6,7,8-

tetrahydro-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 182360-42-5 CAPLUS

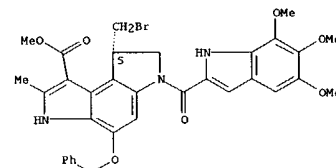
L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,

8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 182360-48-1 CAPLUS

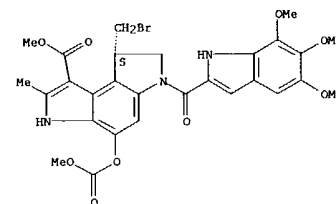
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,

8-(bromomethyl)-3,6,7,8-

tetrahydro-4-[(methoxycarbonyl)oxy]-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.



RN 182360-49-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,

8-(bromomethyl)-3,6,7,8-

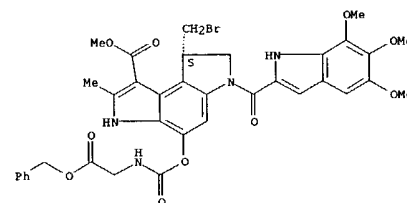
tetrahydro-2-methyl-4-[[[2-oxo-2-(phenylmethoxy)ethyl]amino]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI)

Absolute stereochemistry.

L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

(CA INDEX NAME)

Absolute stereochemistry.



RN 182360-50-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,

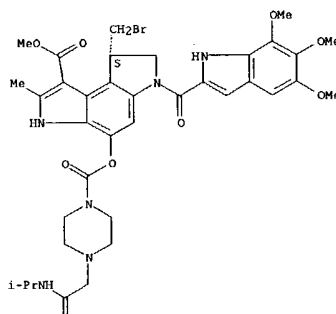
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[4-[2-[(1-methylethyl)amino]-2-oxoethyl]-1-piperazinyl]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

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L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

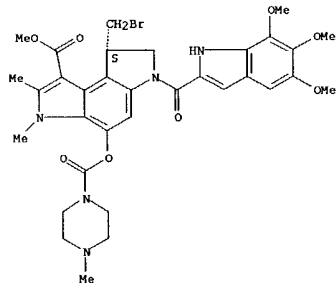
PAGE 2-A



● HCl

RN 182360-52-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-2,3-dimethyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-  
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)-  
(9CI) (CA INDEX NAME)

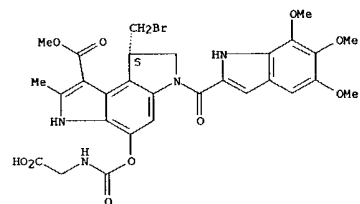
Absolute stereochemistry.



RN 182360-55-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[2-(  
(dimethylamino)ethoxy)-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-  
indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

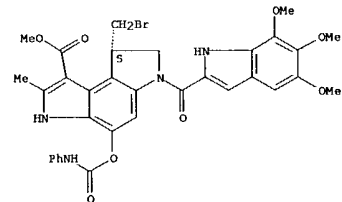
Absolute stereochemistry.

L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 182360-63-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-2-methyl-4-[[[(phenylamino)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-  
indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

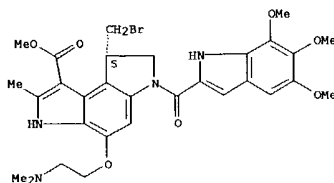
Absolute stereochemistry.



RN 182360-65-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-4-[[[(4-methoxyphenyl)amino]carbonyl]oxy]-2-methyl-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA  
INDEX NAME)

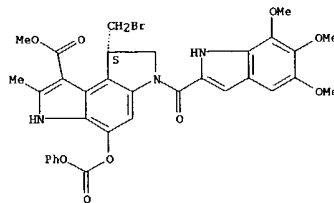
Absolute stereochemistry.

L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 182360-60-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-2-methyl-4-[(phenoxycarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-  
2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

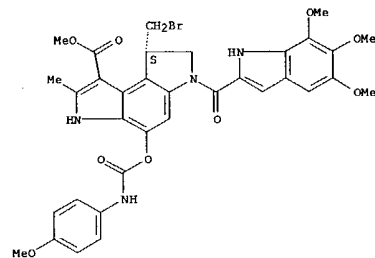
Absolute stereochemistry.



RN 182360-61-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-  
[[[(carboxymethyl)amino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-  
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methyl ester, (S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

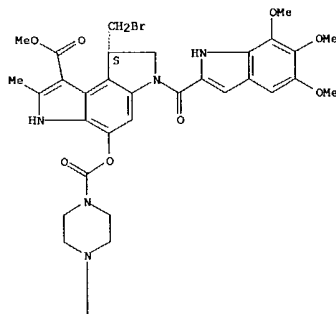
L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 182360-66-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-2-methyl-4-[[[(4-(1-piperidinyl)-1-piperazinyl)carbonyl]oxy]-6-  
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,  
monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



10/069,202

L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



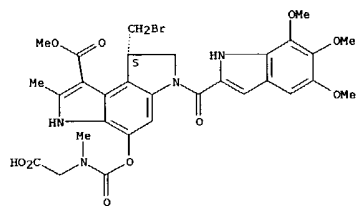
● HCl

RN 182360-67-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-

[[[carboxymethyl]methylamino]carbonyloxy]-3,6,7,8-tetrahydro-2-methyl-6-  
 [(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methyl ester, (S)-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 182360-68-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[5-(4-methyl-1-piperazinyl)-1,5-dioxopentyl]oxy]-6-  
 [(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,  
 monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

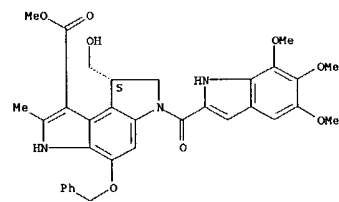
(Reactant or reagent)  
 (synthesis and antitumor activity of A-ring pyrrole analogs of  
 duocarmycin B2)

RN 182360-41-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-

(hydroxymethyl)-2-methyl-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-  
 yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

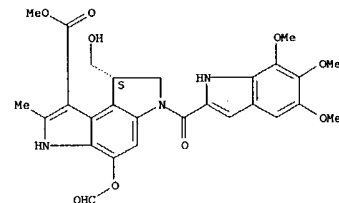


RN 182360-45-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(formyloxy)-3,6,7,8-

tetrahydro-8-(hydroxymethyl)-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-  
 yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

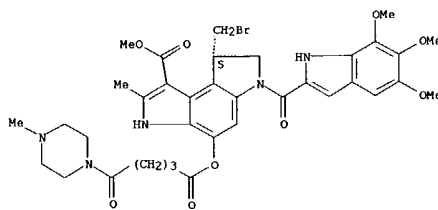
Absolute stereochemistry.



RN 182360-53-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-

L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



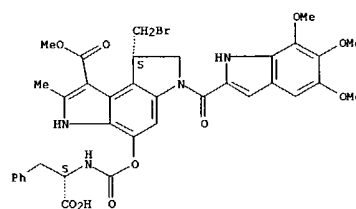
● HCl

RN 182578-89-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[1-

carboxy-2-phenylethyl)amino]carbonyloxy]-3,6,7,8-tetrahydro-2-methyl-6-  
 [(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methyl ester,  
 [S-(R\*,R\*)] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 182360-41-4P 182360-45-8P 182360-53-8P

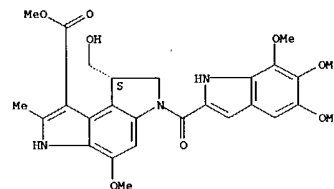
182360-54-9P 182360-58-3P

RE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT

L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

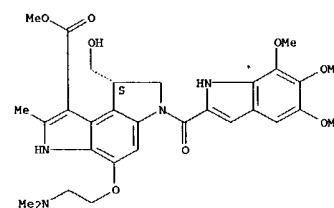


RN 182360-54-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[2-

(dimethylamino)ethoxy]-3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-6-  
 [(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.

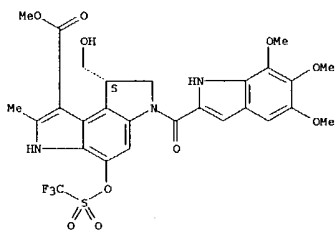


RN 182360-58-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-4-[[[trifluoromethyl]sulfonyloxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

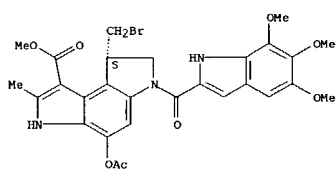
Absolute stereochemistry.

L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

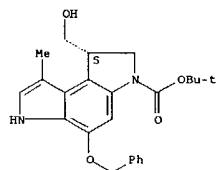


IT 182360-47-0P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (synthesis and antitumor activity of A-ring pyrrole analogs of  
 duocarmycin B2)  
 RN 182360-47-0 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-  
 (bromomethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-  
 yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

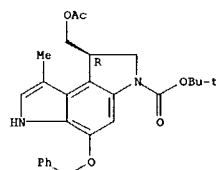


L14 ANSWER 53 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 180081-92-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
 1-[(acetyloxy)methyl]-  
 1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester,  
 (R)- (9CI) (CA INDEX NAME)

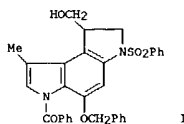
Absolute stereochemistry.



IT 180081-91-8P  
 RL: BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological  
 study); PREP (Preparation); RACT (Reactant or reagent)  
 (enzymic resolution of pyrroloindole precursors of CPI)  
 RN 180081-91-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol,  
 6-benzoyl-1,2,3,6-tetrahydro-8-  
 methyl-5-(phenylmethoxy)-3-(phenylsulfonyl)-, acetate (ester), (R)-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 53 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1996:441562 CAPLUS  
 DN 125:167628  
 TI Enzymic preparation of optically active precursors of CPI, the DNA  
 alkylation subunit of the naturally occurring antitumor antibiotic  
 CC-1065  
 AU Ling, Lei; Low, J. William  
 CS Department Chemistry, University Alberta, Edmonton, T6G 2G2, Can.  
 SO Chemical Communications (Cambridge) (1996), (13), 1559-1560  
 CODEN: CHCOFS; ISSN: 1359-7345  
 PB Royal Society of Chemistry  
 DT Journal  
 LA English  
 GI

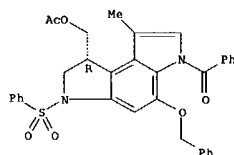


AB Some immediate precursors of CPI were subjected to enzymic resolution  
 with  
 lipase PS in vinyl acetate; racemic pyrroloindole I was effectively  
 resolved by two consecutive enzymic reactions.

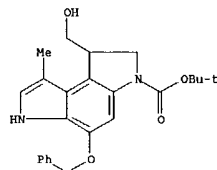
IT 112836-67-6P 180081-92-9P  
 RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP  
 (Preparation)  
 (enzymic resolution of pyrroloindole precursors of CPI)  
 RN 112836-67-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-  
 (hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester,  
 (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 53 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 112089-71-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (enzymic resolution of pyrroloindole precursors of CPI)  
 RN 112089-71-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-  
 (hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester  
 (9CI) (CA INDEX NAME)



10/069,202

L14 ANSWER 54 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:401719 CAPLUS

DN 125:67752

TI Antitumor agent

IN Saito, Hiromitsu; Amishiro, Nobuyoshi; Nagamura, Satoru; Kobayashi, Eiiji

Okamoto, Akihiko; Gomi, Katsushige; Yamashita, Kinya; Sato, Kiyoshi;

Nakakura, Masashi; Hayakawa, Eiiji

PA Kyowa Hakko Kogyo Co., Ltd., Japan

SO PCT Int. Appl., 17 pp.

CODEN: PIXXD2

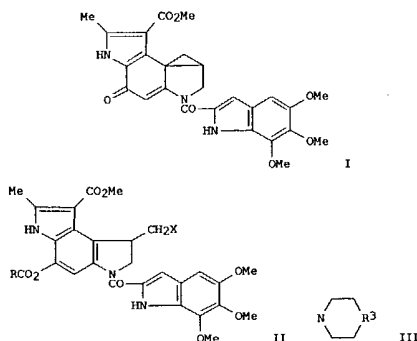
DT Patent

LA Japanese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9610405	A1	19960411	WO 1995-JP1893	19950920
W: AU, CA, CN, FI, HU, JP, KR, NO, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT.				
CA 2201097	AA	19960411	CA 1995-2201097	19950920
AU 9535328	A1	19960426	AU 1995-35328	19950920
EP 786252	A1	19970730	EP 1995-932191	19950920
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL,				
NO 9701409	A	19970520	NO 1997-1409	19970325
FI 9701278	A	19970527	FI 1997-1278	19970326
JP 1994-237226		19940930		
WO 1995-JP1893		19950920		
OS MARPAT 125:67752				
GI				

L14 ANSWER 54 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



AB An antitumor agent against drug-fast tumors comprises a compound represented by general formula (I) or (II) or a pharmacol. acceptable salt thereof as the active ingredient; wherein X represents Cl or Br; and R represents NR1R2 (wherein R1 and R2 represent each independently hydrogen or C1-C4 linear or branched alkyl) or a group of formula (III) (wherein R3 represents CH2 or N-CH3). The agent has an excellent antitumor activity against drug-insensitive tumors and is useful as an antitumor agent against drug-fast tumors. Capsules were formulated containing I 2, Avecel 117.5, and magnesium stearate 0.5 mg.

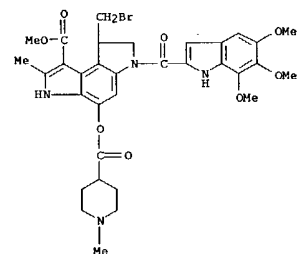
IT 178327-53-2

RL THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antitumor pharmaceutical compns. containing polycyclic compds. as active ingredients)

RN 178327-53-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[1-methyl-4-piperidinyl]carbonyl]oxy]-6-[(5,6,7-

L14 ANSWER 54 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide (9CI)  
(CA INDEX NAME)



● HBr

L14 ANSWER 55 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:368752 CAPLUS

DN 125:114354

TI Synthesis and antitumor activity of novel duocarmycin derivatives

AU Asai, Akira; Nagamura, Satoru; Kobayashi, Eiiji; Gomi, Katsushige;

Saito, Hiromitsu

CS Tokyo Res. Lab., Kyowa Hakko Kogyo Co. Ltd., Tokyo, 194, Japan

SO Bioorganic & Medicinal Chemistry Letters (1996), 6(11), 1215-1220

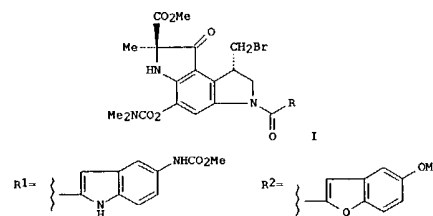
CODEN: BMCLE8; ISSN: 0960-894X

FB Elsevier

DT Journal

LA English

GI



AB A series of Duocarmycin B2 analogs I [R = R1, R2, (E)-CH:CHC6H4OMe-4, (E)-CH:CHC6H4(NHMe)-4, CH2OC6H4OMe-4] bearing simplified right hand segments (Seg-Bs) with the protected phenolic hydroxyl group in left hand segment (Seg-A) was synthesized. Among them, the cinnamoyl derivs. I [R = (E)-CH:CHC6H4OMe-4, (E)-CH:CHC6H4(NHMe)-4] exhibited potent antitumor activity against in vivo murine tumor models in the wider range of doses without detectable toxic effects than DUMB2.

IT 171599-25-0P, Duocarmycin B2 N,N-dimethylcarbamate  
179239-44-2P 179239-46-4P 179239-48-6P  
179239-49-7P 179239-51-1P

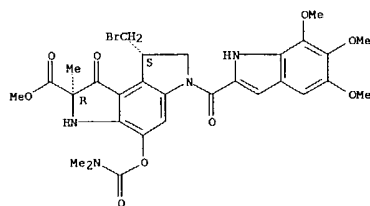
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (synthesis and antitumor activity of novel duocarmycin derivs.)

RN 171599-25-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[[dimethylamino]carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)-(9CI) (CA INDEX NAME)

114 ANSWER 55 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

### Absolute stereochemistry.



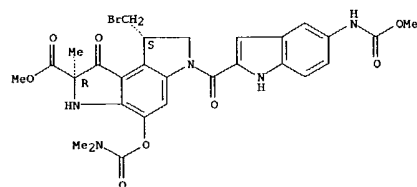
BN 179239-44-2 CAPLUS

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RN      179239-44-2 CAPLUS
CN      Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
        [[ (dimethylamino) carbonyl] oxy]-1,2,3,6,7,8-hexahydro-6-[[5-
        [(methoxycarbonyl) amino]-1H-indol-2-yl] carbonyl]-2-methyl-1-oxo-,
methyl
        ester, (2R-trans)- (9CI) (CA INDEX NAME)

```

Absolute stereochemistry.

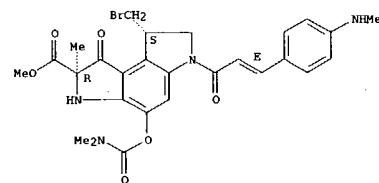


RN 179239-46-4 CAPLUS

RN 1792357-4-4  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-  
 [[dimethylamino]carbonyloxy]-1,2,3,6,7,8-hexahydro-6-[(5-methoxy-2-  
 benzofuranyl)carbonyl]-2-methyl-1-oxo-, methyl ester, (2R-trans-)  
 (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.

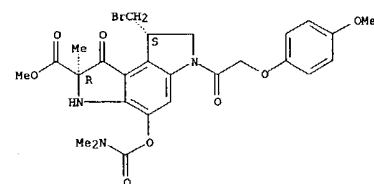
114 ANSWER 55 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



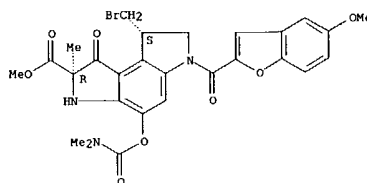
RN 179239-51-1 CAPLUS

RN 179239-51-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-  
 [[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[(4-  
 methoxyphenoxy)acetyl]-2-methyl-1-oxo-, methyl ester, (2R-trans)-  
 (9CI)

Absolute stereochemistry.

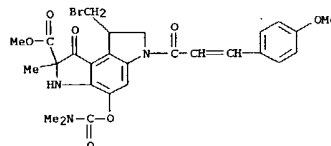


1.14 ANSWER 55 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 179239-48-6 CAPLUS

197239-48-8 CAPLOS  
 Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-  
 [[ (dimethylamino)carbonyloxy]-1,2,3,6,7,8-hexahydro-6-[3-(4-  
 methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-1-oxo-, methyl ester,  
 {2R-[2α,6(E),8β]}- (9CI) (CA INDEX NAME)



BN 179239-49-7 CAPLUS

CN Benzol[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-  
 [[(dimethylamino)carbonyloxy]-1,2,3,6,7,8-hexahydro-2-methyl-6-[3-(4-  
 (methylanilino)phenyl)-1-oxo-2-propenyl]-1-oxo-, methyl ester,  
 [2R-[2 $\alpha$ ,6(E),8 $\beta$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

L14 ANSWER 56 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:325161 CAPLUS

DN 125:58167

TI Wagner-Meerwein rearrangement of duocarmyngins

All Nagamura, Satoru; Kanada, Yutaka; Asai, Akira; Kobayashi, Eiji; Gomi,

AU Nagamura, Satoru; Kanada, Yu  
Katsuhiko; Saito, Hiromitsu

GS Katsushige, Saito, Hiromitsu  
Makino Research Laboratories, Kyushu Hakko Kagaku Co., Ltd. Machida

CS  
194

194, \_\_\_\_\_

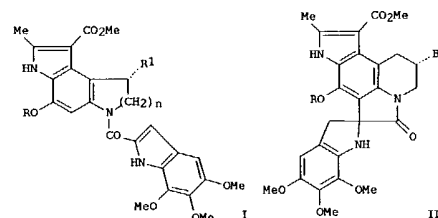
Japan

SO Chemical &amp; Pharmaceutical Bulle

CODEN: C

PB Pharmacology

DT Journal



AB Treatment of 8-O-protected-3-hydroxy derivs. of duocarmycin B2 with camphorsulfonic acid (CSA) in toluene interestingly gave A-ring pyrrole

analogs I [R = SiMe<sub>2</sub>CHMe<sub>3</sub>, CONMe<sub>2</sub>, 4-methylpiperazinecarbonyl (Q), R<sub>1</sub> = CH<sub>2</sub>Br, n = 1]. Their structures were unambiguously elucidated on the basis of NMR and mass spectrometry, and the mechanism was considered

to be a Wagner-Meerwein type rearrangement. On the other hand, treatment of 9-O-protected-3-hydroxy deriva. of duocarmycin BI with CSA afforded different rearrangement products. In the case of bulky groups at the 9-O position, such as a tert-butylidimethylsilyl group, the normal A-ring pyrrole analog I [R = SiMe<sub>2</sub>CMe<sub>3</sub>, R1 = Br, n = 2] was obtained. Under the same conditions, however, the 9-O-N,N-dimethylcarbamoyl-3-hydroxy compound gave the spiro compound II [R = CONMe<sub>2</sub>], which was derived from a 1,2-shift of the methoxycarbonyl group and a bonding between the C-8 position and the C-2' position. The Q-protected compound gave a mixture of I [R = Q, R1 =

10/069,202

L14 ANSWER 56 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
Br, n = 2] and II [R = Q]. I have antitumor activity, whereas II do not.

IT 154089-68-6P 177958-19-9P 177958-20-2P

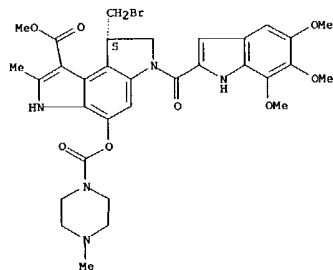
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(Wagner-Meerwein rearrangement of duocarmycins)

RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 177958-19-9 CAPLUS

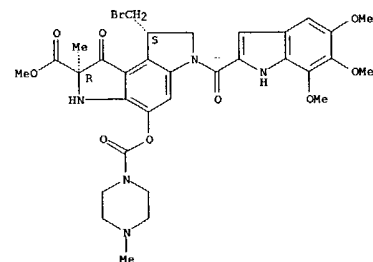
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 56 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.

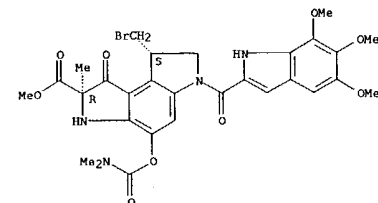


RN 171599-25-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[[(1,1-

[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

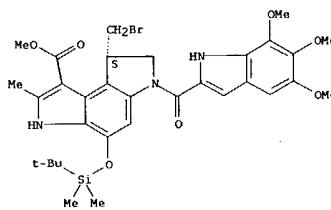


IT 129953-15-7P 129953-17-9P 160819-29-4P

177958-18-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(Wagner-Meerwein rearrangement of duocarmycins)

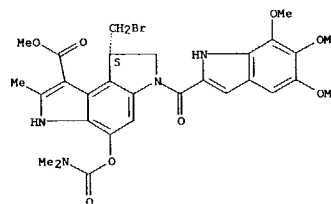
L14 ANSWER 56 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 177958-20-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 154901-65-2 171599-25-0

RL: RCT (Reactant); RACT (Reactant or reagent)  
(Wagner-Meerwein rearrangement of duocarmycins)

RN 154901-65-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-

1,2,3,6,7,8-hexahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

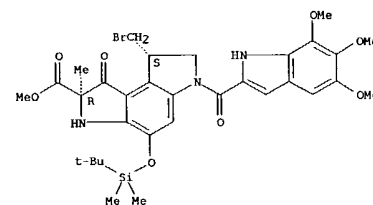
L14 ANSWER 56 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 129953-15-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

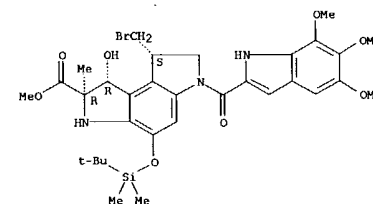


RN 129953-17-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R,2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 160819-29-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-

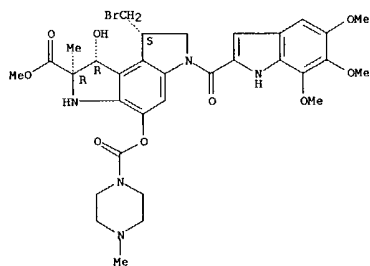


10/069,202

L14 ANSWER 56 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-4-[[4-methyl-1-

piperazinyl)carbonyloxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,  
methyl ester, [1R,2R,8S]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

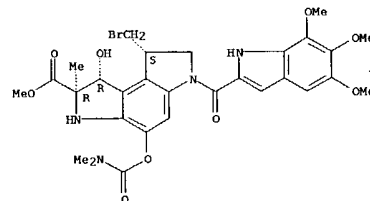


RN 177958-18-8 CAPLUS

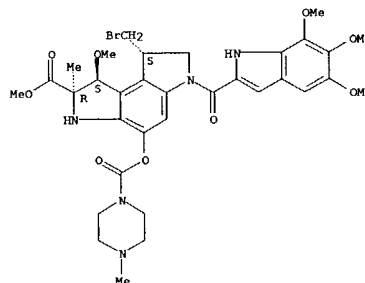
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-

[(dimethylamino)carbonyloxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-6-  
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,  
[1R-(1 $\alpha$ ,2 $\beta$ ,8 $\alpha$ )]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 56 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 56 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT 177958-21-3P 178036-26-5P

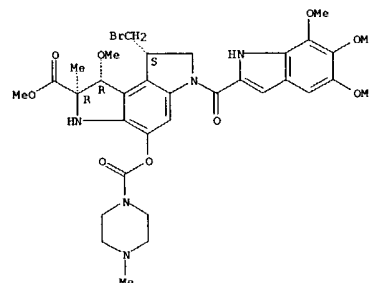
RL: SPN (Synthetic preparation); PREP (Preparation)  
(Wagner-Meerwein rearrangement of duocarmycin)

RN 177958-21-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
1,2,3,6,7,8-hexahydro-1-methoxy-2-methyl-4-[[4-methyl-1-

piperazinyl)carbonyloxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,  
methyl ester, [1R-(1 $\alpha$ ,2 $\beta$ ,8 $\alpha$ )]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

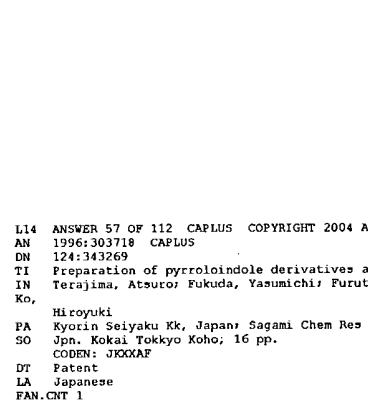


RN 178036-26-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
1,2,3,6,7,8-hexahydro-1-methoxy-2-methyl-4-[[4-methyl-1-

piperazinyl)carbonyloxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,  
methyl ester, [1S-(1 $\alpha$ ,2 $\alpha$ ,8 $\beta$ )]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08034789	A2	19960206	JP 1994-174475	19940726
JP 1994-174475		19940726		
MARPAT 124:343269				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

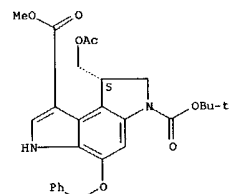
AB The title compds. [I and II; R = C1-4 lower alkyl; R1 =  $\alpha$ -amino acid residue, Q, Q1, Q3, Q4, Q5, Q6, CO-Y-CO; R2 = H, HO-protective group, group degradable in vivo; Y = halo, arylsulfonyloxy, lower alkanesulfonyloxy, haloalkanesulfonyloxy, N3; wherein X1, X2, X3 = H, OH, OR3, O2CR3, CHO, NO2, NR4R5, NR4COR5, NR4CO2R3, Q2, CH2NR4R5, NHCOR4R5; X4, X5, X6 = H, OR3; X7, X13 = O, S, NH; X8, X9, X10, X11, X12, X14 = CH, N; n = 0-2; wherein R3 = (un)substituted linear or branched C1-6 alkyl, (un)substituted aryl; R4, R5 = H, (un)substituted linear or branched C1-6 alkyl, (un)substituted aryl; W = (CH2)m, (CH2)m-24-(CH2)n, Q7; wherein m, n = 0-16; 24 = S, O, NH], optical isomers, and pharmacol. acceptable salts, which show highly selective anticancer activity and low toxicity, are effective against solid tumors, and also have antibacterial activity, are prepared. Thus, 20 mg pyrrolo[3,2-e]indole derivative I (R = Me, R1 = Boc, R2 = H, Y = Cl) (preparation given) was treated with 3 M HCl/EtOAc, stirred for 1 h, and after distilling off the solvent, stirred with 13.2 mg 5,6,7-trimethoxy-1H-indole-2-carboxylic acid and 30.2 mg 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in DMF at room temperature overnight to give 79% I (R = Me, R1 = Q8, R2 = H, Y = Cl). The latter compound (10.6 mg) was suspended in MeCN, treated with 6.2  $\mu$ l 1,8-diazabicyclo[5.4.0]-7-undecene, and stirred at room temperature for 5 h to

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L14 ANSWER 57 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
give the title compd. cyclopropa[c]pyrrolo[3,2-e]indole (7bR,8aS)-II  
(R = Me, R1 = Q8). The title compd. I (R = Me, R1 = Q9, R2 = H, Y = Cl)  
in vitro showed IC50 of 0.048 ng/mL against HeLa S3 cells and at 0.25  
mg/kg in vivo inhibited by 69% the growth of colon 26 cancer cells in mice.  
IT 176685-39-5P 176685-40-8P 176685-41-9P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT

(Reactant or reagent)  
(preparation of pyrrolobenzocarbazolidione and  
cyclopropapyrrolobenzocarbazo  
letrione derivs. as antitumor agents)  
RN 176685-39-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-  
dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 176685-40-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-,  
6-(1,1-dimethylethyl)  
1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

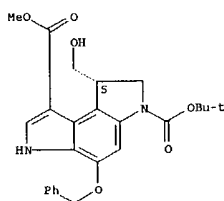
L14 ANSWER 58 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1996:301099 CAPLUS  
DN 124:343266  
TI Preparation of (trifluoromethyl)pyrroloindole and  
-cyclopropapyrroloindole  
derivatives as antitumor agents  
IN Terajima, Atsuro; Fukuda, Yasunichi; Oomori, Yasuo  
PA Kyorin Seiyaku Kk, Japan; Sagami Chem Res  
SO Jpn. Kokai Tokkyo Koho, 14 pp.  
CODEN: JKXXAF  
DT Patent  
LA Japanese  
FAN.CMT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08034786	A2	19960206	JP 1994-174472	19940726
JP 1994-174472		19940726		
MARPAT 124:343266				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

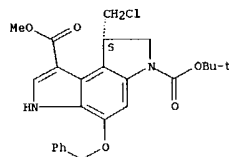
AB The title compds. [I and II; R1 =  $\alpha$ -amino acid residue, Q, Q1, Q3,  
Q4, Q5, Q6, CO-W-CO; R2 = H, HO-protective group, group degradable in  
vivo; Y = halo, arylsulfonyloxy, lower alkanesulfonyloxy,  
haloalkanesulfonyloxy, N3; wherein X1, X2, X3 = H, OH, OR3, O2CR3,  
CHO,  
NO2, NR4R5, NR4COR5, NR4CO2R3, Q2, CH2NR4R5, NHCOR4R5; X4, X5, X6 =  
H,  
OR3; X7, X13 = O, S, NH; X8, X9, X10, X11, X12, X14 = CH, N; n = 0-2;  
wherein R3 = (un)substituted linear or branched C1-6 alkyl,  
(un)substituted aryl; R4, R5 = H, (un)substituted linear or branched  
C1-6  
alkyl, (un)substituted aryl; W = (CH2)m, (CH2)m-Z4-(CH2)n, Q7;  
wherein m,  
n = 0-16; Z4 = S, O, NH], optically active isomers, and pharmacol.  
acceptable salts, which show highly selective anticancer activity  
and low  
toxicity, are effective against solid tumors, and also have  
antibacterial  
activity, are prepared Thus, 11.3 mg pyrrolo[3,2-e]indole  
derivative I (R1 =  
Hoc, R2 = PhCH2, Y = Cl) (preparation given) was dissolved in  
CH2Cl2, treated  
dropwise with a solution of BBr3 in CH2Cl2 (70.5  $\mu$ L, 0.0705 mmol),  
allowed  
to react for 1.75 h, centrifuged to remove the supernatant liquid,  
dried,  
treated with 7.5 mg  
5-(benzofuran-2-carbonyl)amino-1H-indole-2-carboxylic  
acid and 13.5 mg 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide  
hydrochloride, and stirred in DMF for 4.5 h to give 42% I (R1 = Q8).  
The  
latter compound in vitro showed IC50 of 0.49 ng/mL against P388  
cells and at

L14 ANSWER 57 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

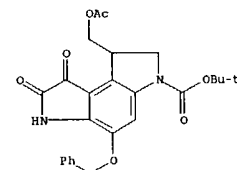


RN 176685-41-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)  
1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

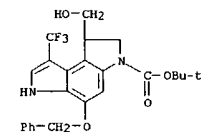
Absolute stereochemistry. Rotation (-).



L14 ANSWER 58 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
0.5 mg/kg in vivo inhibited by 86% the growth of colon 26 cancer  
cells in  
mice.  
IT 132628-62-7  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of (trifluoromethyl)pyrroloindole and  
-cyclopropapyrroloindole  
derivs. as antitumor agents)  
RN 132628-62-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
1-[(acetyloxy)methyl]-  
1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl  
ester  
(9CI) (CA INDEX NAME)



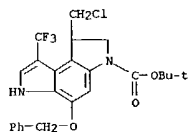
IT 176539-79-0P 176539-80-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT  
(Reactant or reagent)  
(preparation of (trifluoromethyl)pyrroloindole and  
-cyclopropapyrroloindole  
derivs. as antitumor agents)  
RN 176539-79-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-  
(hydroxymethyl)-5-(phenylmethoxy)-8-(trifluoromethyl)-,  
1,1-dimethylethyl  
ester (9CI) (CA INDEX NAME)



RN 176539-80-3 CAPLUS

10/069,202

L14 ANSWER 58 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
1-(chloromethyl)-1,6-  
dihydro-5-(phenylmethoxy)-8-(trifluoromethyl)-, 1,1-dimethylethyl  
ester  
(9CI) (CA INDEX NAME)



L14 ANSWER 59 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1996:248963 CAPLUS  
DN 125:11480  
TI Cyclopropylpyrroloindole-oligopeptide anticancer agents  
IN Lown, J. William; Wang, Yuqiang; Luo, Weide  
PA Synphar Laboratories, Inc., Can.  
SO U.S., 17 pp.  
CODEN: USXXAM

DT Patent  
LA English

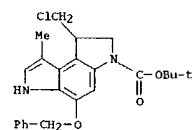
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5502068	A	19960326	US 1995-381355	19950131
CA 2210093	AA	19960808	CA 1996-2210093	19960131
WO 9623497	A1	19960808	WO 1996-US727	19960131
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK,				
EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS,				
LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,				
SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR,				
IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,				
MR, NE				
AU 9649643	A1	19960821	AU 1996-49643	19960131
AU 698001	B2	19981022		
EP 800390	A1	19971015	EP 1996-906176	19960131
EP 800390	B1	20021204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,				
PT, IE				
JP 11500427	T2	19990112	JP 1996-523576	19960131
AT 228837	E	20021215	AT 1996-906176	19960131
PRAI US 1995-381355	A	19950131		
WO 1996-US727	W	19960131		
OS MARPAT 125:11480				
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The invention is directed to novel  
cyclopropylpyrroloindole-oligopeptide  
comps. which are useful as anticancer agents. The novel  
cyclopropylpyrroloindole-oligopeptide comps. have the following  
general  
structure: I wherein, Het1 and Het2 are individually selected from the  
group consisting of pyrrole, imidazole, N-alkylimidazole,  
N-alkoxymethylimidazole, thiophene, thiophene, furan, thiazole,  
oxazole,

L14 ANSWER 59 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
N-alkylpyrrole, N-alkoxymethylpyrrole and pyrrole, R is selected  
from the  
group consisting of a valence bond; a divalent C1-C6 alkyl; a  
divalent  
C2-C6 alkenyl; a divalent C2-C6 alkynyl; a divalent cycloalkane of  
formula  
CpH2p-2 wherein p is 3 to 7; and an ortho, meta or para linked arom.  
group, A is selected from the group consisting of a C1-C6 alkyl  
group; an  
amidine or deriv. thereof; a guanidine; a secondary, tertiary or  
quaternary ammonium salt; and a sulfonium salt, n is 0 to 3, and m  
is 0 to  
3, wherein when n=0, m is 1-3. Thus, e.g., deprotection of  
5-benzyloxy-3-tert-butylloxycarbonyl-1-chloromethyl-8-methyl-1,2-dihydro-3H-  
pyrrolo[3,2-e]indole (III) followed by coupling with  
4-(4-butyramido-N-  
methyl-2-pyrrolocarboxyamido)-N-methyl-2-pyrrolocarboxylic acid and ring  
closure afforded  
(E)-1,2,8,8a-tetrahydro-7-methyl-2-[4-(4-butyramido-N-  
methyl-2-pyrrolocarboxyamido)-N-methyl-2-pyrrolocarboxyl]cyclopropa[c]pyrr  
olo[3,2-e]indole-4-(5H)-one ((E)-III) which exhibited cytotoxicity  
of TD50  
= 9.50 + 10-10 µg/mL for KB human nasopharyngeal tumor cells  
(TD50 = 1 + 10-6 µg/mL for CC-1065). A detailed anal. of the  
frequency of occurrence of bases flanking the prominent DNA  
alkylation  
sites for III is given and compared with CC-1065, providing evidence  
of  
the main cellular event that gives rise to the expression of  
anticancer  
properties of the new drugs and how they differ in detail from  
CC-1065.  
IT 175614-07-0  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(cyclopropylpyrroloindole-oligopeptide anticancer agents)  
RN 175614-07-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
1-(chloromethyl)-1,6-  
dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI)  
(CA  
INDEX NAME)

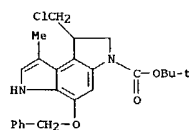


L14 ANSWER 59 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

10/069,202

L14 ANSWER 60 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1996:185423 CAPLUS  
 DN 124:278276  
 TI Design, synthesis, cytotoxic properties and preliminary DNA sequencing  
 evaluation of CPI-N-methylpyrrole hybrids. Enhancing effect of a trans double bond linker and role of the terminal amide functionality on cytotoxic potency  
 AU Wang, Yuqiang; Gupta, Rajan; Huang, Liren; Luo, Weide; Lown, J. William  
 CS Dep. of Chemistry, Univ. of Alberta, Edmonton, AB, T6G 2G2, Can.  
 SO Anti-Cancer Drug Design (1996), 11(1), 15-34  
 CODEN: ACDDEN; ISSN: 0266-9536  
 PB Oxford University Press  
 DT Journal  
 LA English  
 AB In an approach to the design and exploration of the properties of cyclopropylindole (CPI)-lexitropsin conjugates as potential anticancer agents, CPI-N-methylpyrroles of two sep. classes have been synthesized and characterized. These comprise structures (i) in which the N-methylpyrrole moiety bears amide groups of different sizes and (ii) in which both flexible and rigid linkers are introduced between the CPI and N-methylpyrrole units. The extent and the relative rates of DNA cleavage following alkylation and thermal treatment by these CPI conjugates were determined by an agarose gel mobility shift assay. The DNA sequence preferences of the 7 new agents were also determined in a preliminary study by high-resolution polyacrylamide gel electrophoresis and contrasted with that of CC-1065. The CPI-N-methylpyrrole agents avoid the major alkylation sites of CC-1065, but all alkylate the minor CC-1065 site of 5'AATA and exhibit a consensus sequence of 5'-N.A/T.A/T.A. The cytotoxicities of these compds. were determined against KB human tumor cells in vitro. Compound 6, bearing a 4-butyramide group in the N-methylpyrrole, is 100 times more potent than 7 which lacks an amide group, while 10 which bears a rigid trans double bond linker is 100 times more potent than its flexible ethyl-linked counterpart.  
 IT 175614-07-0  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (design, synthesis, cytotoxic properties and preliminary DNA sequencing)

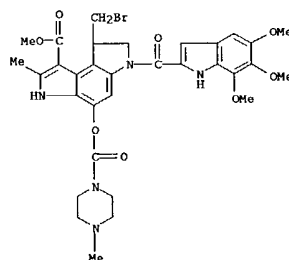
L14 ANSWER 60 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 evaluation of cyclopropylindole-N-methylpyrrole hybrids)  
 RN 175614-07-0 CAPLUS  
 CH Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI)  
 (CA INDEX NAME)



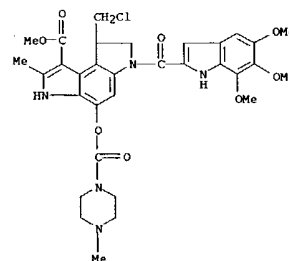
L14 ANSWER 61 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1996:115202 CAPLUS  
 DN 124:156002  
 TI Method for stabilizing duocarmycin derivatives  
 IN Nakakura, Masashi; Ueno, Fujii; Hayakawa, Elji; Kuroda, Tokuyuki  
 PA Kyowa Hako Kogyo Co., Ltd., Japan  
 SO PCT Int. Appl., 16 pp.  
 CODEN: PIXX02  
 DT Patent  
 LA English  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9531971	A1	19951130	WO 1995-JP962	19950519
W: AU, BR, CA, CN, CZ, FI, HU, KR, MX, NO, NZ, PL, RO, RU, SI, SK, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 07309761	A2	19951128	JP 1994-106415	19940520
CA 2190635	AA	19951130	CA 1995-2190635	19950519
AU 9524551	A1	19951218	AU 1995-24551	19950519
EP 754030	A1	19970122	EP 1995-918749	19950519
EP 754030	B1	20001220		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1148805	A	19970430	CN 1995-193164	19950519
BR 9507640	A	19970819	BR 1995-7640	19950519
HU 78072	A2	19990830	HU 1996-3521	19950519
AT 198149	E	20010115	AT 1995-918749	19950519
US 5703080	A	19971230	US 1996-737145	19961030
NO 9604813	A	19961113	NO 1996-4813	19961113
FI 9604624	A	19961119	FI 1996-4624	19961119
PRAI JP 1994-106415	A	19940520		
WO 1995-JP962	W	19950519		
OS MARPAT 124:156002				
AB Stabilized duocarmycin derivs. are prepared by adding at least a compound selected from the group consisting of saccharides, electrolytes, water-soluble polymers, polyhydric alcs. and surfactants to a solution containing the duocarmycin derivs. Also provided are freeze-dried pharmaceutical preps. containing the stabilized duocarmycin derivs. Citric acid 50, duocarmycin-HBr (I) 100, and lactose 5000 mg were dissolved in distilled water to make a total volume of 200 mL. The resulting solution was placed into vials in 2 mL portions, and freeze-dried under reduced pressure. After storage at 60° for 30 days, HPLC anal. showed that 100% of I remained. IT 134106-78-8 134106-81-3 173552-35-7 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (freeze-dried preps. containing stabilized duocarmycin derivs.) RN 134106-78-8 CAPLUS CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-[(5,6,7-				

L14 ANSWER 61 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 134106-81-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

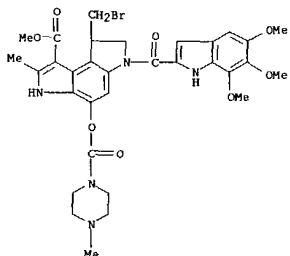


RN 173552-35-7 CAPLUS

10/069,202

L14 ANSWER 61 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-[[5,6,7-trimethoxy-1H-indol-2-yl]carbonyl]-, methyl ester, monohydrobromide, monohydrate (9CI) (CA INDEX NAME)



PAGE 1-A

● HBr

PAGE 2-A

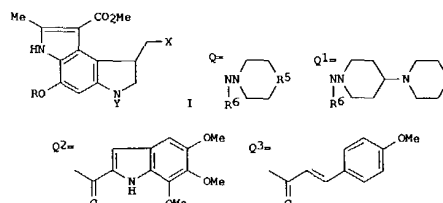
● H<sub>2</sub>O

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1995:998395 CAPLUS  
 DN 124:176153  
 TI Preparation of DC-89 derivatives as antitumor agents  
 IN Amishiro, Nobuyoshi; Nagamura, Satoru; Saito, Hiromitsu; Kobayashi, Ei-ji

PA Kyowa Hakko Kogyo Co., Ltd., Japan  
 SO PCT Int. Appl., 58 pp.  
 CODEN: PIRX02

DT Patent  
 LA Japanese  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9529179	A1	19951102	WO 1995-JP779	19950420
W: AU, CA, JP, KR, US				
HW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2165819	AA	19951102	CA 1995-2165819	19950420
AU 9522671	A1	19951116	AU 1995-22671	19950420
AU 685939	B2	19980129		
EP 705833	A1	19960410	EP 1995-916020	19950420
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 5641780	A	19970624	US 1995-564178	19951215
PRAI JP 1994-84714	A	19940422		
WO 1995-JP779	W	19950420		
OS MARPAT 124:176153				
GI				



AB DC-89 derivs. (I; X = Cl or Br; R = (un)substituted alkyl, (un)substituted

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 aralkyl, COR1, OR2, SR2, NR3R4, Q, Q1, S02R8; wherein R1 = H, (un)substituted alkyl, aryl, or heterocyclyl; R2 = (un)substituted alkyl.

aryl; R3, R4 = H, (un)substituted alkyl, NH2, mono- or dialkylamino; provided that R3 = R4 = H; R5 = NR7, O; R6, R7 = H, (un)substituted alkyl; R8 = (un)substituted alkyl or aryl; Y = Q2, Q3) or pharmacol. acceptable salts thereof are prep. Thus, the tert-butyl dimethylsilyl ether I (R = Me3CSiMe2, X = Br, Y = Q2) (50 mg) was dissolved in THF, treated with 0.11 mL 1.0 M Bu4NF/THF, and stirred at room temp. for 1 h to give, after workup, the alc. I (R = H, X = Br, Y = Q2) which was dissolved in MeCN, treated with 48% aq. HBr, stirred at room temp. for 1 h, treated with 1 N aq. HBr, and extd. with CHCl3. The CHCl3 ext. was dried over anhyd. Na2SO4 and evapd. to dryness to give the crude product which was dissolved in CH2Cl2, treated with 0.027 mL Ph chloroformate and 0.030 mL Et3N, and stirred at -78° to 0° for 1 h to give, after workup and silica gel chromatog., the title pyrroloindoline I (R = CO2Ph, X = Br, Y = Q2). The latter compd. in vitro showed IC50 of 0.051 nM for inhibiting the proliferation of HeLaS3 cells and in vivo exhibited T/C of 0.090 (tumor vol. of the treated animal/tumor vol. of the control) in mice transplanted with sarcoma 180.

IT 173903-48-5P 173903-49-6P 173903-50-9P

173903-51-0P 173903-52-1P 173903-53-2P

173903-54-3P 173903-55-4P 173903-56-5P

173903-57-6P 173903-58-7P 173903-59-8P

173903-60-1P 173903-61-2P 173903-62-3P

173903-63-4P 173903-64-5P 173903-65-6P

173903-66-7P 173903-67-8P 173903-68-9P

173903-69-0P 173903-70-3P 173903-71-4P

173903-72-5P 173903-73-6P 173903-74-7P

173903-75-8P 173903-76-9P 173903-77-0P

173903-78-1P 173903-79-2P 173903-80-3P

173903-81-6P 173903-82-7P 173903-83-8P

173903-84-9P 173903-85-0P 173903-86-1P

173903-87-2P

RL BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

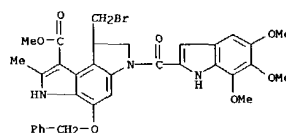
BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of DC-89 (pyrroloindoline) derivs. as antitumor agents)

RN 173903-48-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

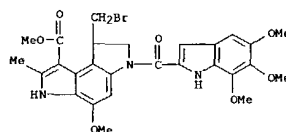
tetrahydro-2-methyl-4-(phenylmethoxy)-6-[[5,6,7-trimethoxy-1H-indol-2-

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



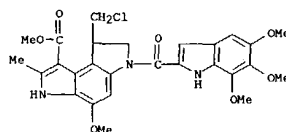
RN 173903-49-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-

tetrahydro-4-methoxy-2-methyl-6-[[5,6,7-trimethoxy-1H-indol-2-yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 173903-50-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-methoxy-2-methyl-6-[[5,6,7-trimethoxy-1H-indol-2-yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

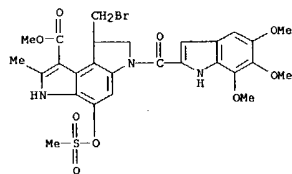


RN 173903-51-0 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-

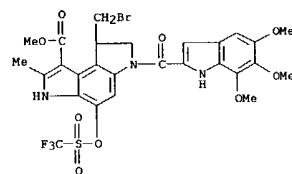
10/069,202

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

tetrahydro-2-methyl-4-[(methylsulfonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

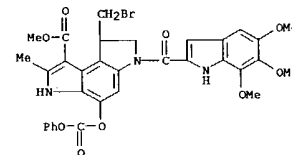


RN 173903-52-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[trifluoromethylsulfonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

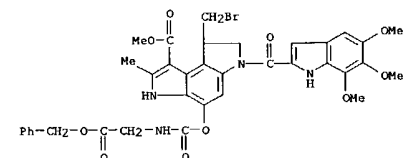


RN 173903-53-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

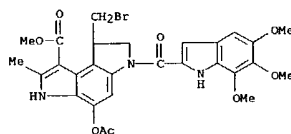


RN 173903-56-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[2-oxo-2-(phenylmethoxy)ethyl]amino]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



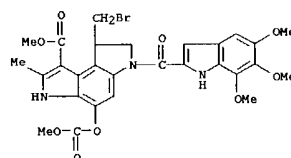
RN 173903-57-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(carboxymethyl)amino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173903-54-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

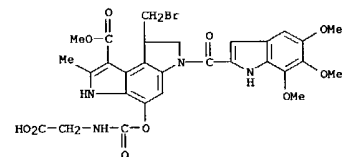
tetrahydro-4-[(methoxycarbonyl)oxy]-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



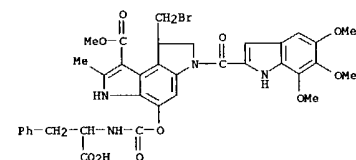
RN 173903-55-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[(phenoxycarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

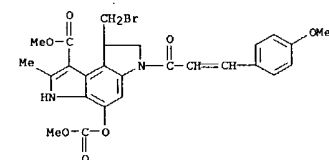
L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173903-58-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(1-carboxy-2-phenylethyl)amino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methyl ester (9CI) (CA INDEX NAME)

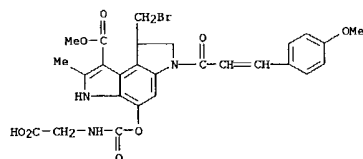


RN 173903-59-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[(methoxycarbonyl)oxy]-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

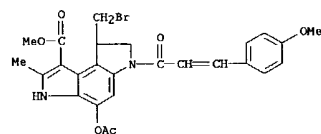


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L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 RN 173903-60-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-  
 [[(carboxymethyl)amino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-  
 methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, 1-methyl ester (9CI) (CA  
 INDEX NAME)

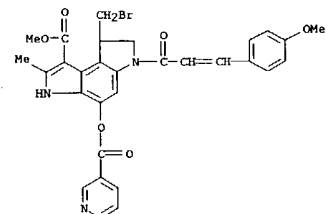


RN 173903-61-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-  
 (bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-  
 2-methyl-, methyl ester (9CI) (CA INDEX NAME)



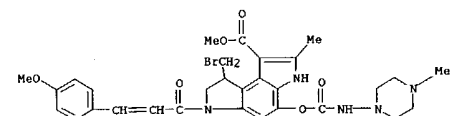
RN 173903-62-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-  
 tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-  
 [(methylthio)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



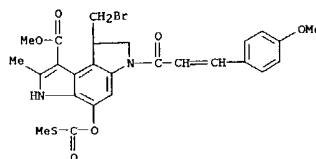
● HCl

RN 173903-65-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-  
 tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-  
 methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester (9CI) (CA  
 INDEX NAME)

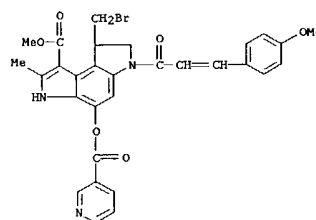


RN 173903-66-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-  
 tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-  
 methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester,  
 monohydrochloride  
 (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

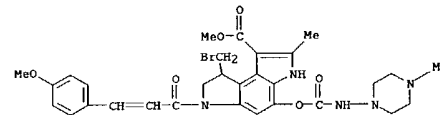


RN 173903-63-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-  
 tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(3-  
 pyridinylcarbonyl)oxy]-, methyl ester (9CI) (CA INDEX NAME)



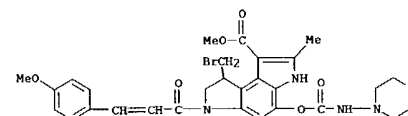
RN 173903-64-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-  
 tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(3-  
 pyridinylcarbonyl)oxy]-, methyl ester, monohydrochloride (9CI) (CA  
 INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



● HCl

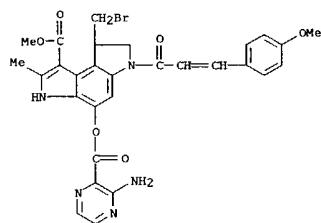
RN 173903-67-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-  
 tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-  
 morpholinylamino)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



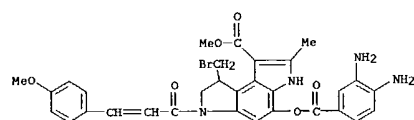
RN 173903-68-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[(3-  
 aminopyrazinyl)carbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-  
 methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA  
 INDEX NAME)

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L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



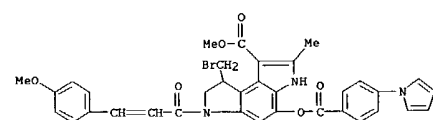
RN 173903-69-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[[3,4-  
diaminobenzoyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-  
propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



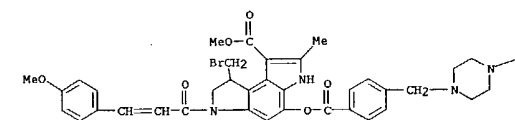
RN 173903-70-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[[4-  
(dimethylamino)benzoyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-  
oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 173903-73-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-(1H-  
pyrrol-1-yl)benzoyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

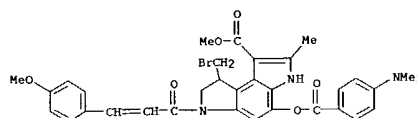


RN 173903-74-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-(4-  
methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester (9CI) (CA  
INDEX NAME)

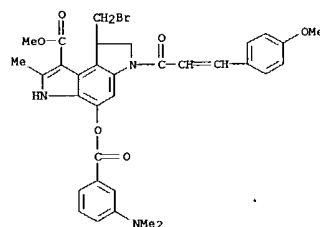


RN 173903-75-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-(4-  
methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester,  
monohydrobromide

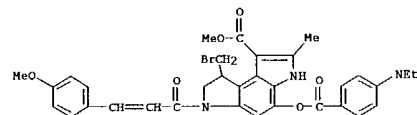
L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



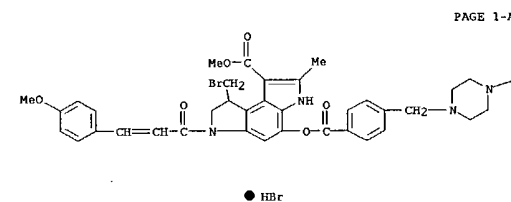
RN 173903-71-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[3-  
(dimethylamino)benzoyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-  
oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



RN 173903-72-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[4-  
(diethylamino)benzoyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-  
2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

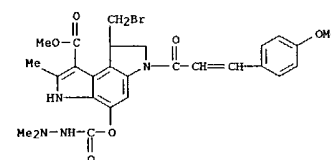


PAGE 1-A

PAGE 1-B

RN 173903-76-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[[2,2-  
dimethylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-  
1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

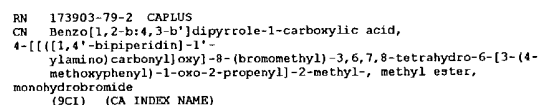
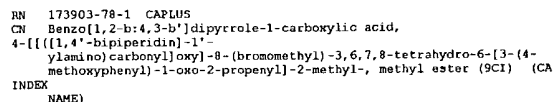
Me



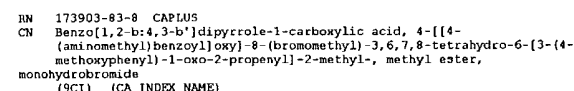
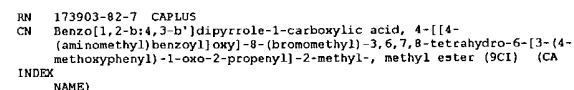
RN 173903-77-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-  
[[[trimethylhydrazino)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX  
NAME)



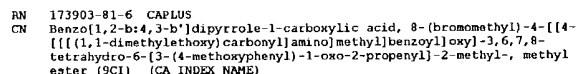
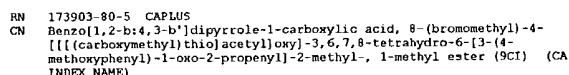
114 ANSWER 62 OF 112 CAPIJIS COPYRIGHT 2004 ACS on STN (Continued)



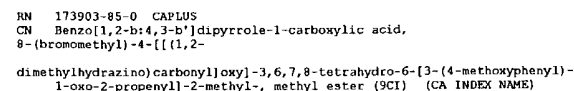
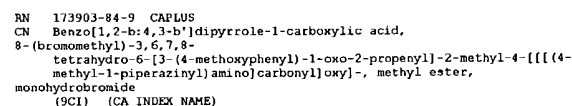
L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

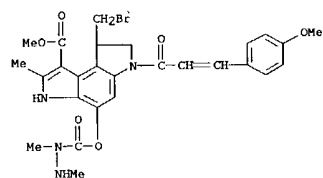


L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

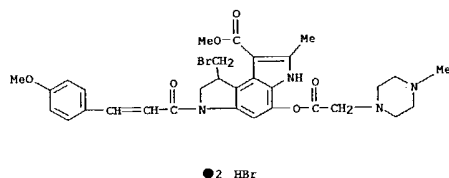


10/069,202

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



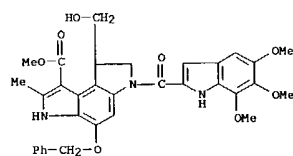
RN 173903-86-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-methyl  
-1-piperazinyl]acetyl]oxy]-, methyl ester, dihydrobromide (9CI) (CA  
INDEX NAME)



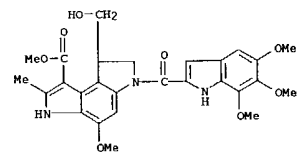
● 2 HBr

RN 173903-87-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
4-[[1,4'-bipiperidin]-1'-  
ylacetyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-  
oxo-2-propenyl]-2-methyl-, methyl ester, dihydrobromide (9CI) (CA  
INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

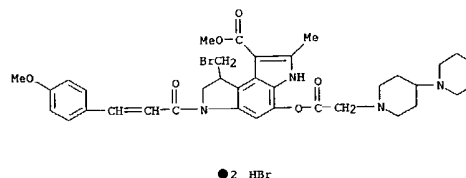


RN 173903-90-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-  
(hydroxymethyl)-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-  
yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



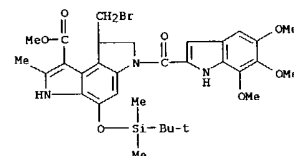
RN 173903-91-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[[[2-  
(1,1-dimethylethoxy)-2-oxoethyl]amino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-  
[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI)  
(CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



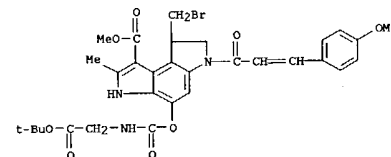
● 2 HBr

IT 134127-18-7  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of DC-89 (pyrroloindoline) derivs. as antitumor  
agents)  
RN 134127-18-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[[[1,1-  
dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX  
NAME)



IT 173903-89-4P 173903-90-7P 173903-91-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT (Reactant or reagent)  
(preparation of DC-89 (pyrroloindoline) derivs. as antitumor  
agents)  
RN 173903-89-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-  
(hydroxymethyl)-2-methyl-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-  
(hydroxymethyl)-2-methyl-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-

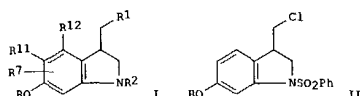
L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



10/069,202

L14 ANSWER 63 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1995:997014 CAPLUS  
 DN 124:145899  
 TI Preparation of 6-hydroxyindoline acetals and analogs as cytostatic prodrugs  
 IN Tietze, Lutz F.  
 FA Germany  
 SO Ger. Offen., 39 pp.  
 CODEN: GWXXRX  
 DT Patent  
 LA German  
 FAN. CNT 1

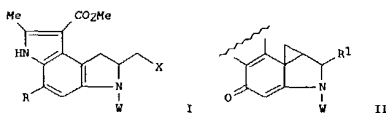
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 4415463	A1	19951109	DE 1994-4415463	19940503
DE 4415463	C2	19960926		
PRAI DE 1994-4415463		19940503		
OS MARPAT 124:145899				
GI				



AB Title compds. [I; R = CR4(OR3)CHR5R6, R8; R1 = halo, alkylsulfonyloxy, OSO2Ph, etc.; R2 = (un)substituted alkyl, alkylsulfonyloxy, Ac, alkoxycarbonyl, etc.; R3 = (un)substituted alkyl, hydroxy-protective group, sugar residue; R4-R7 = H, (un)substituted alkyl; R8 = sugar residue; R11, R12 = H; R11R12 = NR10CH:CR9; R9, R10 = H, alkyl] were prepared  
 Thus, hydroxyindoline II (R = H) (preparation given) was condensed with CH2:CHOEt to give II (R = CHMeOEt) which gave pH 6.2 growth of bronchial carcinoma cells A 549 47.14% of control at 3.0µg/mL in vitro.  
 IT 173368-66-6P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of 6-hydroxyindoline acetals and analogs as cytostatic prodrugs)  
 RN 173368-66-6 CAPLUS

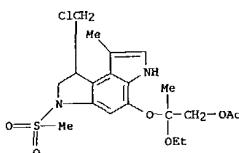
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1995:99646 CAPLUS  
 DN 124:116964  
 TI Preparation of DC-89 derivatives as antitumors  
 IN Amishiro, Nobuyoshi; Nagamura, Satoru; Saito, Hiromitsu; Kobayashi, Eiji  
 OKamoto, Akihiko; Gomi, Katsushige  
 FA Kyowa Hakko Kogyo Co., Ltd., Japan  
 SO PCT Int. Appl., 93 pp.  
 CODEN: PIXXDZ  
 DT Patent  
 LA Japanese  
 FAN. CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9526964	A1	19951012	WO 1995-JP626	19950331
SE AU 9520848	A1	19951023	AU 1995-20848	19950331
AU 689566	B2	19980402		
EP 702014	A1	19960320	EP 1995-913398	19950331
PT, SE 5670492	A	19970923	US 1995-557055	19951128
PRAI JP 1994-65236		19940401		
WO 1995-JP626		19950331		
OS MARPAT 124:116964				
GI				

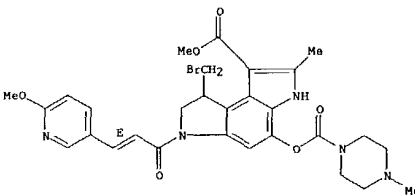


AB DC-89 derivs. e.g. I [W = heterocyclylalkenoyl, arylalkenoyl, etc.; X = Cl, Br; R = acyloxy, 4-alkylpiperazin-1-ylamino] and II (R1 = H, CH2-X; X and W same as above) and their pharmaceutically acceptable salts, having excellent antitumor activity and useful as antitumor drugs, are prepared  
 Thus, a mixture of II [W = R1 = H] was reacted with p-nitrophenyl (E)-3-(6-methoxy-3-pyridinyl)acrylate in DMF containing NaH at -20° for 2 h to give 78% II [W = (E)-3-(6-methoxy-3-pyridinyl)acryloyl, R1 = H].  
 This at 1.0 mg/Kg i.v. had an IC50 of 0.42 nM against sarcoma 180 tumors

L14 ANSWER 63 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 CN Benzo[1,2-b:4,3-b']dipyrrole,  
 5-[2-(acetyloxy)-1-ethoxy-1-methylethoxy]-1-(chloromethyl)-1,2,3,6-tetrahydro-8-methyl-3-(methylsulfonyl)- (9CI)  
 (CA INDEX NAME)



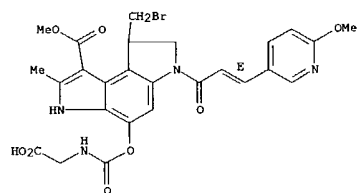
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 IT 173087-75-7P 173087-76-8P 173087-78-0P  
 173087-80-4P 173087-82-6P 173087-84-8P  
 173087-86-0P 173087-90-6P 173087-93-9P  
 173087-95-1P 173087-96-2P 173087-98-4P  
 173087-99-5P 173088-00-1P 173088-01-2P  
 173088-02-3P 173088-03-4P 173088-04-5P  
 173088-05-6P 173088-06-7P 173088-07-8P  
 173088-08-9P 173088-09-0P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (preparation of duocarmycin B1 derivs. as antitumors)  
 RN 173087-75-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(6-methoxy-3-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)  
 Double bond geometry as shown.



RN 173087-76-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(6-methoxy-3-pyridinyl)-1-oxo-2-propenyl]-2-methyl-, 1-methyl ester, (E)- (9CI)  
 (CA INDEX NAME)  
 Double bond geometry as shown.

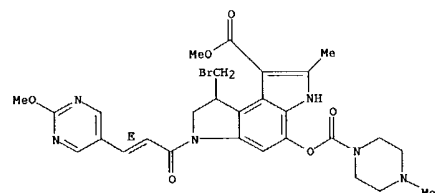
10/069,202

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



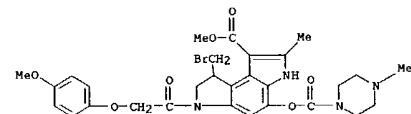
RN 173087-78-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-  
[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, (E)- (9CI)  
(CA INDEX NAME)

Double bond geometry as shown.

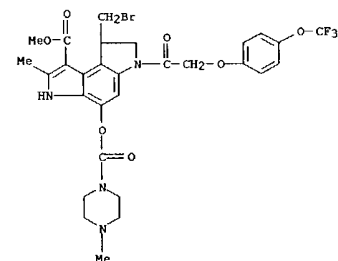


RN 173087-80-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-6-[3-(6-methoxy-3-pyridazinyl)-1-oxo-2-propenyl]-2-methyl-4-  
[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, (E)- (9CI)  
(CA INDEX NAME)

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173087-86-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-[[4-(  
trifluoromethoxy)phenoxy]acetyl]-, methyl ester (9CI) (CA INDEX  
NAME)

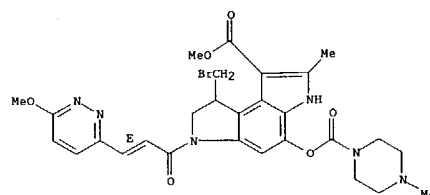


RN 173087-90-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
6-[3-(3-(3-aminopropoxy)-4-  
methoxyphenyl)-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-  
methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, (E)-  
(9CI) (CA INDEX NAME)

Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

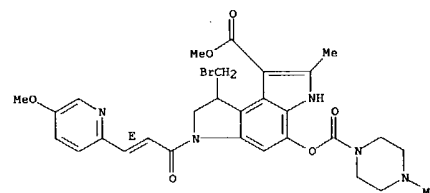
Double bond geometry as shown.



RN 173087-82-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

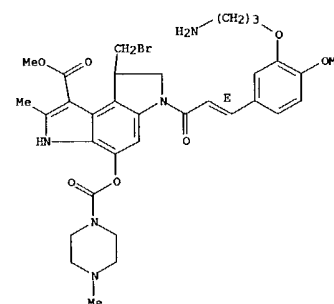
tetrahydro-6-[3-(5-methoxy-2-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[4-  
methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, (E)- (9CI) (CA  
INDEX NAME)

Double bond geometry as shown.



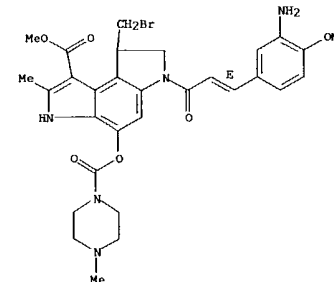
RN 173087-84-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-6-[[4-methoxyphenoxy]acetyl]-2-methyl-4-[[[4-methyl-1-  
piperazinyl]carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173087-93-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-(3-amino-4-  
methoxyphenyl)-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-  
methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, (E)-  
(9CI) (CA INDEX NAME)

Double bond geometry as shown.



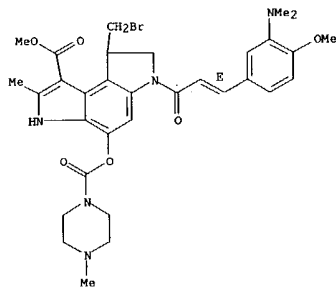
RN 173087-95-1 CAPLUS

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L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-6-[3-[3-

(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

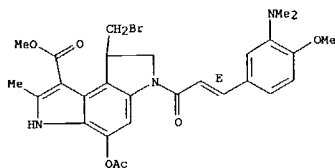
Double bond geometry as shown.



RN 173087-96-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

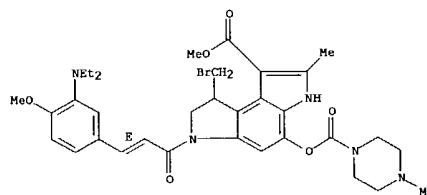
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173087-98-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-

(diethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

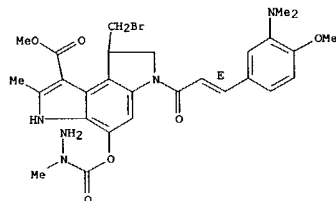
Double bond geometry as shown.



RN 173087-99-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[1-methylhydrazino]carbonyl]oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

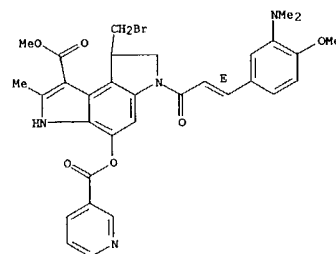
Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173088-00-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[3-pyridinylcarbonyl]oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

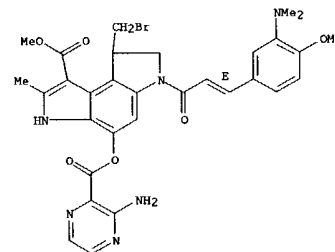
Double bond geometry as shown.



RN 173088-01-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[3-aminopiperazinyl]carbonyl]oxy]-8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

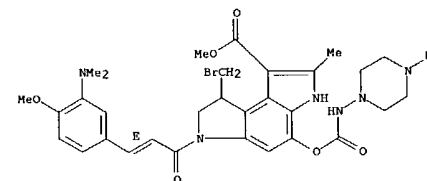
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173088-02-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-

(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]amino]carbonyl]oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

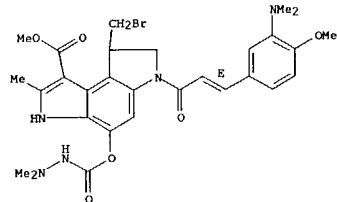


RN 173088-03-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-4-[[[2,2-dimethylhydrazino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

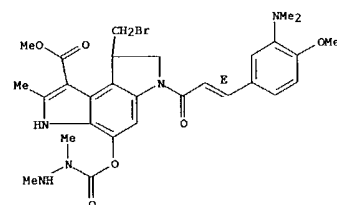
10/069,202

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173088-04-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-4-[[1,2-dimethylhydrazino]carbonyloxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

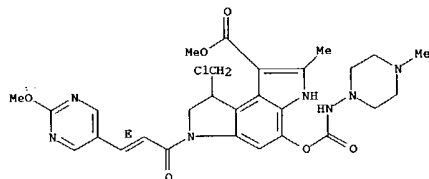
Double bond geometry as shown.



RN 173088-05-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyloxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

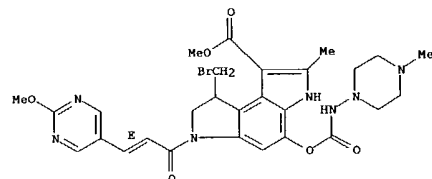
Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173088-07-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyloxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

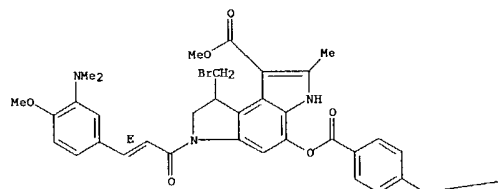
Double bond geometry as shown.



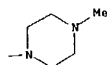
RN 173088-08-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)methyl]benzoyloxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
PAGE 1-A



PAGE 1-B

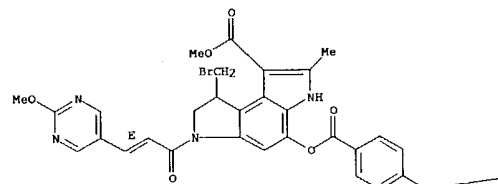


RN 173088-06-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyloxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

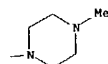
Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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PAGE 1-B

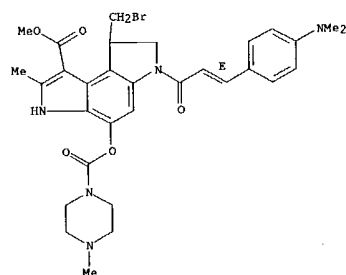


RN 173088-09-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-6-[3-[4-(dimethylamino)phenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyloxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

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L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 173088-10-3P 173088-11-4P 173088-12-5P  
173088-13-6P 173088-14-7P 173088-15-8P  
173088-16-9P 173088-17-0P 173088-18-1P  
173088-21-6P 173088-24-9P 173088-27-2P  
173088-28-3P 173088-29-4P 173088-30-7P  
173088-31-8P 173088-32-9P 173088-33-0P  
173088-34-1P 173088-35-2P 173088-36-3P  
173088-37-4P 173088-38-5P 173088-39-6P  
173088-40-9P 173088-41-0P 173088-42-1P  
173088-43-2P 173088-44-3P 173088-45-4P  
173088-46-5P 173088-47-6P 173088-48-7P  
173088-49-8P 173088-50-1P 173088-51-2P  
173088-52-3P 173088-55-6P 173088-56-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of duocarmycin BI derivs. as antitumors)

RN 173088-10-3 CAPLUS

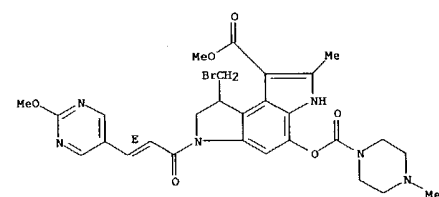
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(6-methoxy-3-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
(E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



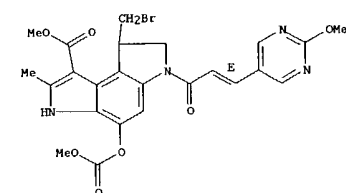
● HCl

RN 173088-13-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-4-[(methoxycarbonyl)oxy]-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

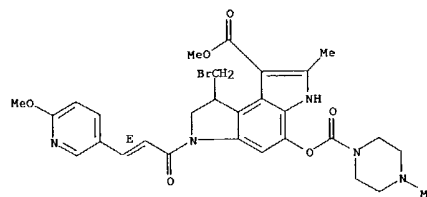


RN 173088-14-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-

[[[(carboxymethyl)amino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-, 1-methyl ester, (E)- (9CI) (CA INDEX NAME)

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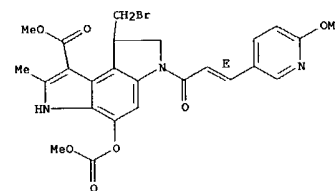
● HCl

RN 173088-11-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-4-[(methoxycarbonyl)oxy]-6-[3-(6-methoxy-3-pyridinyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



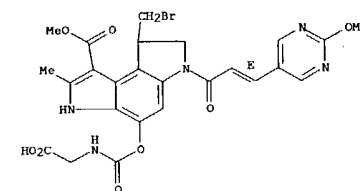
RN 173088-12-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, monohydrochloride,

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
INDEX NAME)

Double bond geometry as shown.

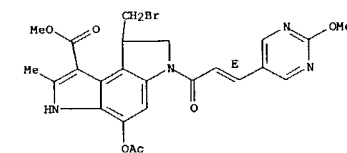


RN 173088-15-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-

(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 173088-16-9 CAPLUS

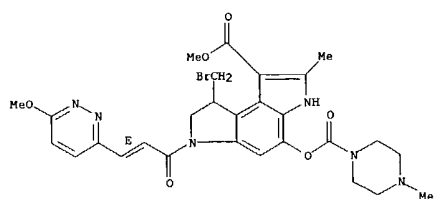
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(6-methoxy-3-pyridazinyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

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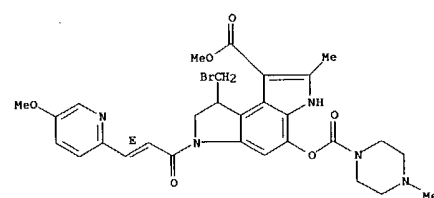


● HCl

RN 173088-17-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(5-methoxy-2-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



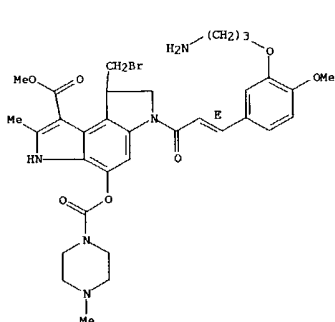
● HCl

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 173088-24-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
6-[3-(3-aminopropoxy)-4-

methoxyphenyl]-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, dihydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



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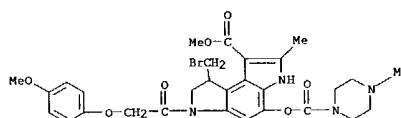
● 2 HCl

RN 173088-27-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-6-[3-[3-(carboxymethyl)-4-methoxyphenyl]-1-oxo-2-propenyl]-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, 1-methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

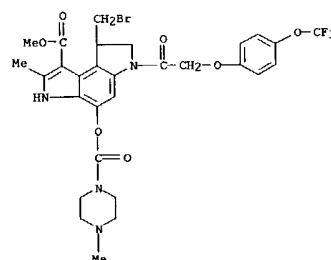
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 173088-18-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-tetrahydro-6-[[4-methoxyphenoxy]acetyl]-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



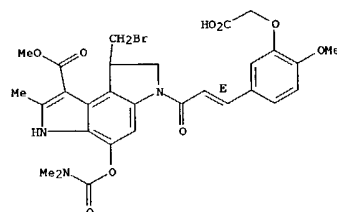
● HCl

RN 173088-21-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-[[4-(trifluoromethoxy)phenoxy]acetyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



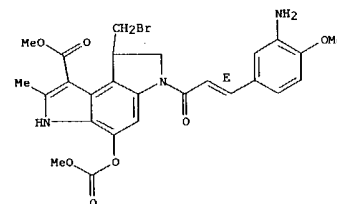
● HCl

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RN 173088-28-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-(3-amino-4-methoxyphenyl)-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-4-[[[methoxycarbonyl]oxy]-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 173088-29-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-(3-amino-4-methoxyphenyl)-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, dihydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

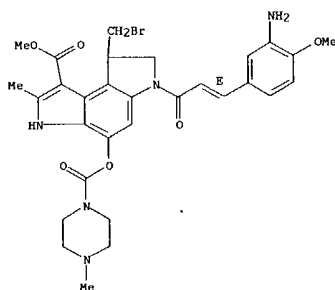
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●2 HCl

RN 173088-30-7 CAPLUS

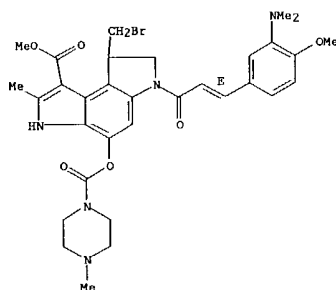
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-

(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyloxy]-, methyl ester, dihydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

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●2 HCl

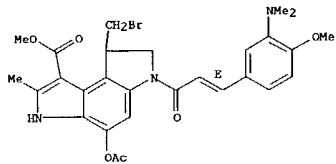
RN 173088-31-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-

3,6,7,8-tetrahydro-2-methyl-, methyl ester, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



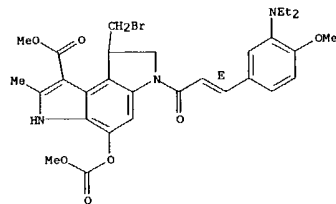
● HCl

RN 173088-32-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-

(diethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-4-[(methoxycarbonyloxy)-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



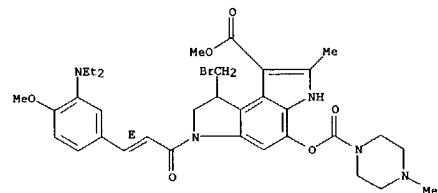
RN 173088-33-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-

(diethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyloxy]-, methyl ester, dihydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



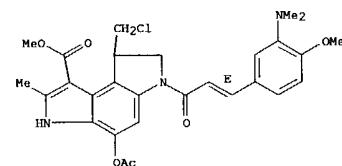
●2 HCl

RN 173088-34-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-

3,6,7,8-tetrahydro-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 173088-35-2 CAPLUS

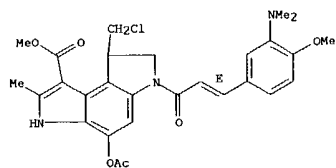
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-

3,6,7,8-tetrahydro-2-methyl-, methyl ester, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

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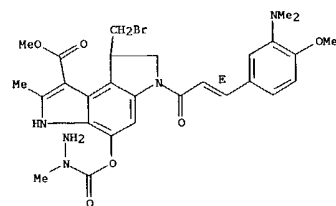


● HCl

RN 173088-36-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-

(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[1-methylhydrazino)carbonyl]oxy]-, methyl ester, monohydrobromide, (E)- (9CI) (CA INDEX NAME)

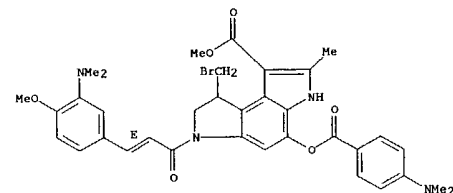
Double bond geometry as shown.



● HBr

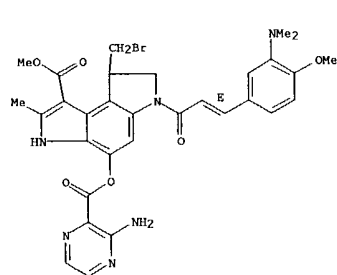
RN 173088-37-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173088-39-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[3-aminopyrazinyl)carbonyl]oxy]-8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, dihydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



● 2 HBr

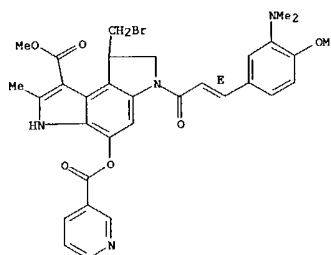
RN 173088-40-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[3-pyridinylcarbonyl]oxy]-, methyl ester, dihydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



● 2 HBr

PAGE 2-A

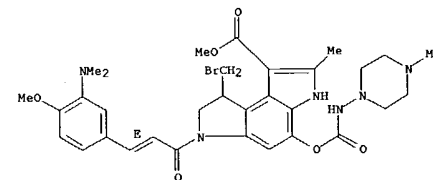
RN 173088-38-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[4-(dimethylamino)benzoyl]oxy]-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl)amino)carbonyl]oxy]-, methyl ester, dihydrobromide, (E)- (9CI) (CA INDEX NAME)

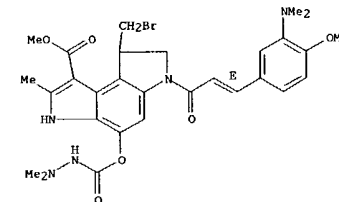
Double bond geometry as shown.



● 2 HBr

RN 173088-41-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-4-[[[2,2-dimethylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, monohydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



● HBr

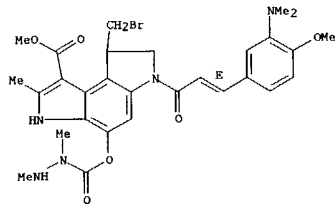
PAGE 1-A

PAGE 2-A

10/069,202

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 RN 173088-42-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-6-[3-(3-(dimethylamino)-4-methoxyphenyl)-1-oxo-2-propenyl]-4-[[1,2-dimethylhydrazino]carbonyloxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, monohydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



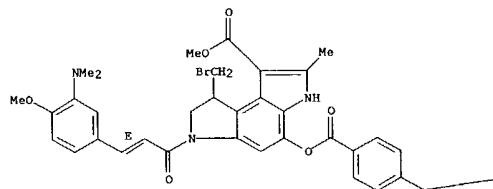
● HBr

RN 173088-43-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-6-[3-(3-(dimethylamino)-4-methoxyphenyl)-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[4-(4-methyl-1-piperazinyl)methyl]benzoyloxy]-, methyl ester, dihydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

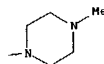
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



● 2 HBr

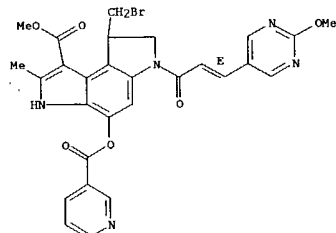
PAGE 1-B



RN 173088-44-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[3-(pyridinylcarbonyloxy)-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

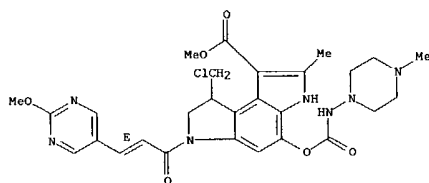
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173088-45-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(chloromethyl)-3,6,7,8-

tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyloxy]-, methyl ester, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



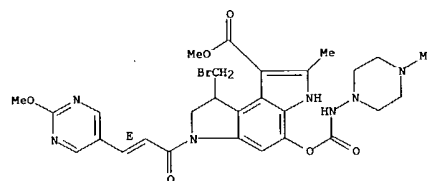
● HCl

RN 173088-46-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyloxy]-, methyl ester, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Double bond geometry as shown.

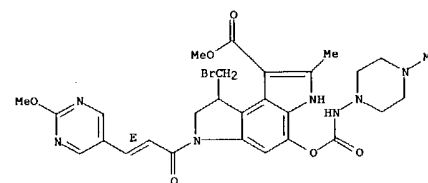


● HCl

RN 173088-47-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyloxy]-, methyl ester, monohydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



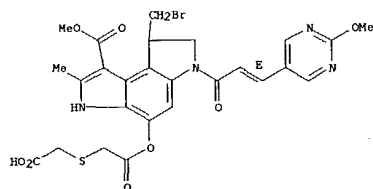
● HBr

RN 173088-48-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(carboxymethyl)thio]acetyl]oxy]-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-, 1-methyl ester, (E)- (9CI) (CA INDEX NAME)

10/069,202

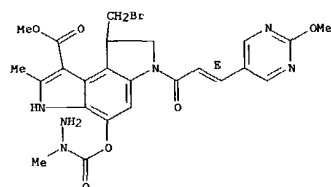
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
INDEX NAME)

Double bond geometry as shown.



RN 173088-49-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-4-{{[1-(  
 methylhydrazino)carbonyl]oxy}-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-  
 pyridinidyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (E)- (9CI)  
 (CA  
 INDEX NAME)

Double bond geometry as shown.

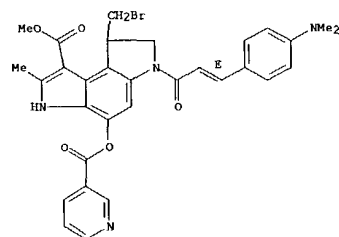


RN 173088-50-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[4

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

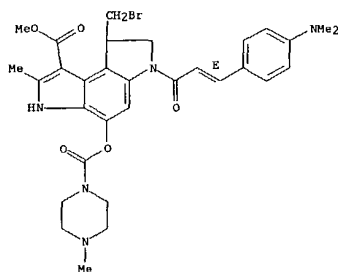
Double bond geometry as shown.



RN 173088-S2-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-6-[3-[4-

(dimethylamino)phenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-  
[[ (4-methyl-1-piperazinyl) carbonyl]oxy]-, methyl ester,  
monohydrobromide,  
(E)- (9CI) (CA INDEX NAME)

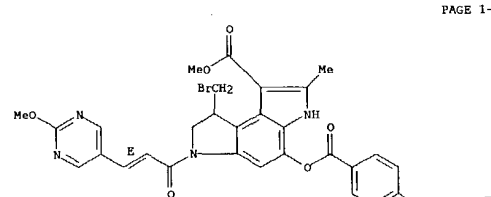
Double bond geometry as shown.



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L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester,  
monohydrobromide, (E)- (9CI) (CA INDEX NAME)

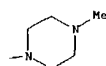
Double bond geometry as shown.



● HBГ

PAGE 1-A

PAGE 1-B



RN 173088-51-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-6-[3-(4-

(dimethylamino)phenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

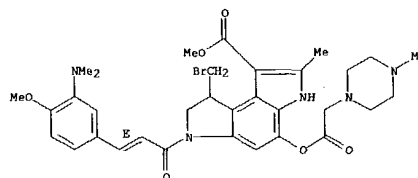
PAGE 2-A



RN 173088-55-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-6-[3-(3-

(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl)acetyl]oxy]-, methyl ester, trihydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



●3 HB $\pi$

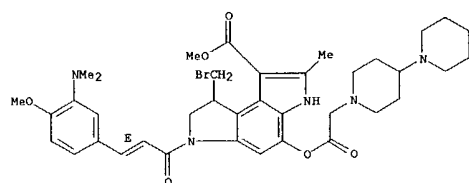
RN 173088-56-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
4-[(1,4'-bipiperidin)-1'-

ylacetyl oxy]-8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-2-methyl-, methyl ester, trihydrobromide, (E)- (9CI)  
(CA  
INDEX NAME)

Double bond geometry as shown.

10/069,202

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



● 3 HBr

L14 ANSWER 65 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:926111 CAPLUS

DN 123:340084

TI Pyrrolo[3,2-e]indole derivatives, process for their preparation, and applications as antitumor agents

IN Delamano Garcia, Jose; Tojo Suarez, Gabriel; Lopez Goti, Carmen; Fernandez

PA Almeida, Jesus; Garcia Gravalos, Dolores; Faircloth, Glynn Thomas

SO Universidad de Santiago de Compostela, Spain

SO PCT Int. Appl., 45 pp.

CODEN: PIXXD2

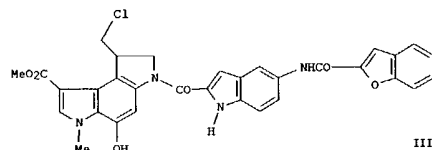
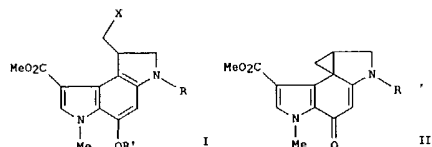
DT Patent

LA Spanish

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9514022	A1	19950526	WO 1994-ES122	19941118
	W: JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	ES 2074957	A1	19950916	ES 1993-2430	19931119
	ES 2074957	B1	19960616		
	EP 680964	A1	19951108	EP 1995-900773	19941118
	EP 680964	B1	20020116		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL,				
PT, SE	JP 08509990	T2	19961022	JP 1994-514236	19941118
	AT 212023	E	20020215	AT 1995-900773	19941118
	PT 680964	T	20020628	PT 1995-900773	19941118
	ES 2171521	T3	20020916	ES 1995-900773	19941118
	US 6786377	A	19980728	US 1997-790904	19970129
PRAI	ES 1993-2430	A	19931119		
	ES 1993-243	A	19930209		
	WO 1994-ES122	W	19941118		
	US 1996-491870	A1	19960515		
OS	CASREACT 123:340084; MARPAT 123:340084				
GI					

L14 ANSWER 65 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



AB New pyrrolo[3,2-e]indole derivs. of formulas I and II are claimed

[wherein

R = COR''; R' = (un)substituted aryl or heteroaryl; R' = H,

(un)substituted alkanoyl, alkenoyl, alkynoyl, (hetero)arenocarbonyl;

X = Cl, bromo, iodo, alkyl- or arylsulfonyl]. The compds. are prepared

by: (a) deacetylating II (R = Ac) to give II (R = H); (b) subjecting the

latter to a cyclopropyl ring-opening reaction to give I.HX (R = R' = H); (c)

reacting this with an acid R''CO<sub>2</sub>H to yield I (R = COR'', R' = H);

(d) optionally reacting I with a base in the presence of a condensing

agent to obtain II; (e) optionally reacting I with a carboxylic acid in the

presence of a condensing agent or with an acid chloride in the

presence of a base to give I (R' = acyl). I and II are useful as antitumor

agents.

For example, deacylation of II (R = Ac) with NaOMe in MeOH gave 99%

II (R = H), which was cleaved by anhydrous HCl in EtOAc to give 93% I.HCl

(R = R' = H, X = Cl). Coupling of this with

5-[(benzofuran-2-ylcarbonyl)amino]-1H-

indole-2-carboxylic acid in DMF in the presence of

Et<sub>3</sub>N:C(N(CH<sub>2</sub>)<sub>3</sub>NMe<sub>2</sub>).HCl

gave 69% title compound III. In the P388 tumor model in mice, III

at 0.5

L14 ANSWER 65 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

mg/kg/day i.p. for 9 days gave at treated/control survival ratio of >

391%.

IT 170431-06-8P

RL: BYP (Byproduct); RCT (Reactant); PREP (Preparation); RACT

(Reactant or

reagent)

(byproduct; preparation of pyrroloindole derivs. as antitumor

agents)

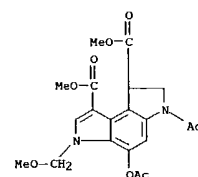
RN 170431-06-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,8-dicarboxylic acid,

3-acetyl-5-(acetyloxy)-

1,2,3,6-tetrahydro-6-(methoxymethyl)-, dimethyl ester (9CI) (CA INDEX

NAME)



IT 170430-99-6P 170431-00-2P 170431-01-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(intermediate; preparation of pyrroloindole derivs. as antitumor

agents)

RN 170430-99-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,8-dicarboxylic acid,

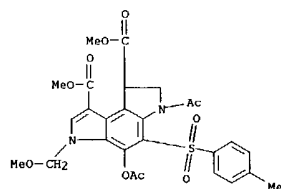
3-acetyl-5-(acetyloxy)-

1,2,3,6-tetrahydro-6-(methoxymethyl)-4-[(4-methylphenyl)sulfonyl]-,

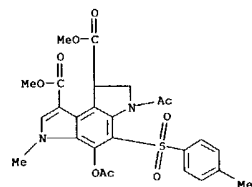
dimethyl ester (9CI) (CA INDEX NAME)

10/069,202

L14 ANSWER 65 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

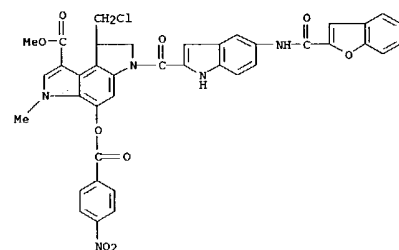


RN 170431-00-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1,8-dicarboxylic acid,  
3-acetyl-5-(acetyloxy)-  
1,2,3,6-tetrahydro-6-methyl-4-[(4-methylphenyl)sulfonyl]-, dimethyl  
ester (9CI) (CA INDEX NAME)

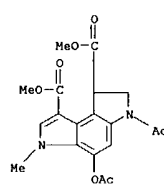


RN 170431-01-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1,8-dicarboxylic acid,  
3-acetyl-5-(acetyloxy)-  
1,2,3,6-tetrahydro-6-methyl-, dimethyl ester (9CI) (CA INDEX NAME)

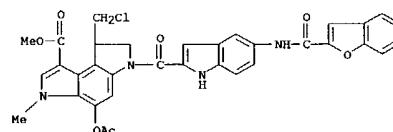
L14 ANSWER 65 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 65 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

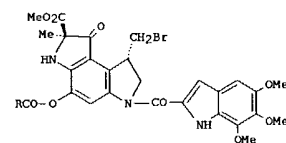


IT 170430-96-3P 170430-97-4P  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological  
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic  
use);  
BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of pyrroloindole derivs. as antitumor agents)  
RN 170430-96-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
4-(acetyloxy)-6-[[5-[(2-  
benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-  
3,6,7,8-tetrahydro-3-methyl-, methyl ester (9CI) (CA INDEX NAME)



RN 170430-97-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-  
benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-  
3,6,7,8-tetrahydro-3-methyl-4-[(4-nitrobenzoyl)oxy]-, methyl ester  
(9CI) (CA INDEX NAME)

L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1995:902197 CAPLUS  
DN 124:29479  
TI Synthesis and antitumor activity of duocarmycin derivatives  
AU Nagamura, Satoru; Kanda, Yutaka; Kobayashi, Eiji; Gomi, Katsushige;  
Saito,  
Hiromitsu  
CS Kyowa Hakkō Kogyo Co., Ltd., Tokyo Res. Lab., Tokyo, 194, Japan  
SO Chemical & Pharmaceutical Bulletin (1995), 43(9), 1530-5  
CODEN: CPBTAL; ISSN: 0009-2363  
PB Pharmaceutical Society of Japan  
DT Journal  
LA English  
OS CASREACT 124:29479  
GI



I

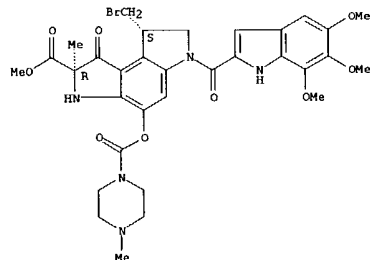
AB A series of duocarmycin B2 derivs. I [R = morpholino-,  
4-Mepiperazinyl-CO(CH<sub>2</sub>)<sub>n</sub>, morpholinyl(CH<sub>2</sub>)<sub>n</sub>, PhCH<sub>2</sub>COCONH(CH<sub>2</sub>)<sub>n</sub>, Me<sub>2</sub>N,  
4-Mepiperazinyl, morpholino, piperazinyl, pyrrolidinyl, MeNH, PhNH; n  
= 1-4], modified at the phenolic hydroxyl group to ester, carbonate and  
carbamate, was synthesized. Antitumor activity of these analogs was  
preliminarily evaluated by assays of growth inhibition of HeLa S3  
cells  
(in vitro) and antitumor activity against murine sarcoma 180 (in  
vivo).  
The stability of the compds. under aqueous conditions was examined,  
and we found  
a correlation between antitumor activity in vivo and stability in  
aqueous  
solution, i.e., the more stable derivs. exhibited higher antitumor  
activity.  
Among these derivs., the N,N-dialkylcarbamoyl analogs exhibited both  
improved antitumor activity and higher stability compared with  
duocarmycin  
B2. These analogs were subjected to further biol. evaluation and they  
expressed broad-spectrum activity toward murine solid tumors M5076,  
Colon  
26 and Colon 38, and human xenografted carcinoma MX-1.  
IT 154901-65-2P 171524-41-7P 171524-44-0P  
171599-18-1P 171599-19-2P 171599-20-5P

10/069,202

L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

171599-21-6P 171599-22-7P 171599-23-8P  
171599-25-0P 171599-26-1P 171599-27-2P  
171599-29-4P 171599-30-7P  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation);  
BIOL (Biological study); PREP (Preparation)  
(synthesis, stability and antitumor activity of duocarmycin  
derivs.)  
RN 154901-65-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
1,2,3,6,7,8-hexahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-1-  
oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,  
(2R,8S)- (9CI) (CA INDEX NAME)

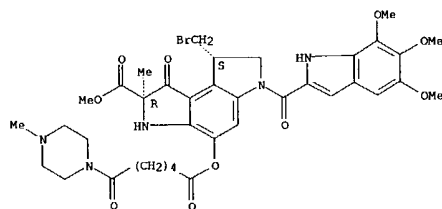
Absolute stereochemistry.



RN 171524-41-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
1,2,3,6,7,8-hexahydro-2-methyl-4-[[[6-(4-methyl-1-piperazinyl)-1,6-  
dioxohexyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,  
methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

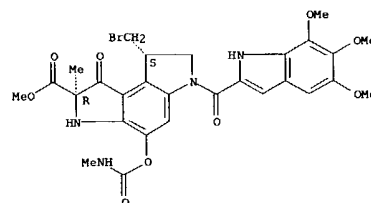
Absolute stereochemistry.

L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 171524-44-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
1,2,3,6,7,8-hexahydro-2-methyl-4-[[[methylamino]carbonyl]oxy]-1-oxo-6-  
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)-  
(9CI) (CA INDEX NAME)

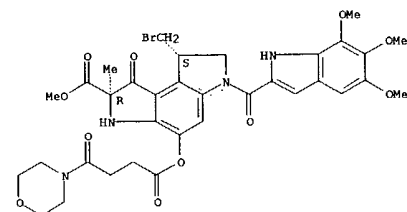
Absolute stereochemistry.



RN 171599-18-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
1,2,3,6,7,8-hexahydro-2-methyl-4-[[[4-morpholinyl]-1,4-dioxobutoxy]-1-oxo-  
6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,  
(2R-trans)- (9CI) (CA INDEX NAME)

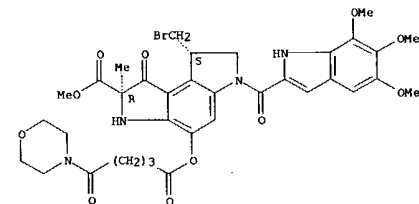
Absolute stereochemistry.

L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 171599-19-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
1,2,3,6,7,8-hexahydro-2-methyl-4-[[[5-(4-morpholinyl)-1,5-dioxopentyl]oxy]-  
1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,  
(2R-trans)- (9CI) (CA INDEX NAME)

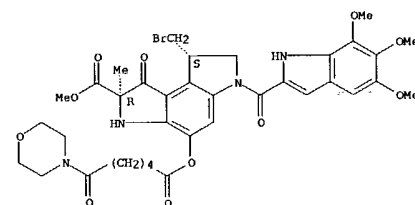
Absolute stereochemistry.



RN 171599-20-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
1,2,3,6,7,8-hexahydro-2-methyl-4-[[[6-(4-morpholinyl)-1,6-dioxohexyl]oxy]-1-  
oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,  
(2R-trans)- (9CI) (CA INDEX NAME)

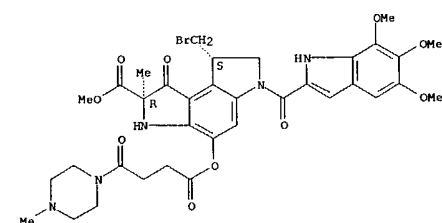
Absolute stereochemistry.

L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 171599-21-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
1,2,3,6,7,8-hexahydro-2-methyl-4-[[[4-(4-methyl-1-piperazinyl)-1,4-  
dioxobutoxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,  
methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

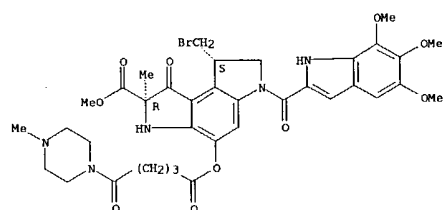


RN 171599-22-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
1,2,3,6,7,8-hexahydro-2-methyl-4-[[[5-(4-methyl-1-piperazinyl)-1,5-  
dioxopentyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,  
methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/069,202

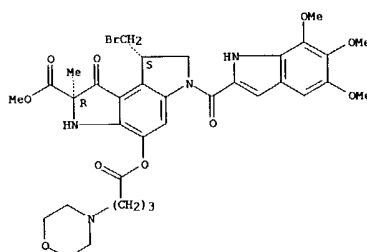
L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



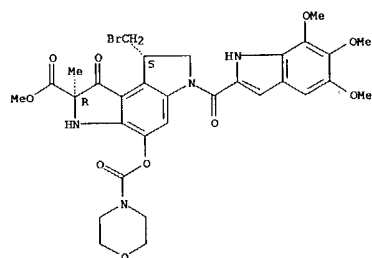
RN 171599-23-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[(4-morpholinyl)-1-oxobutoxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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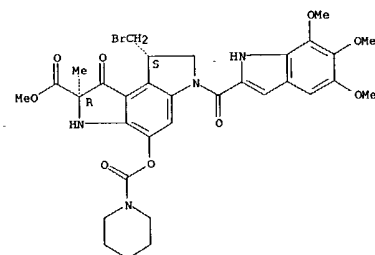


L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 171599-27-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[(1-piperidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 171599-29-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

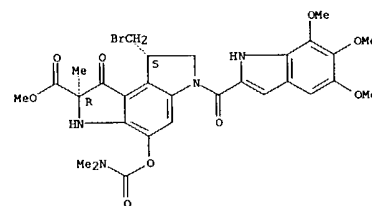
L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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● HCl

RN 171599-25-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



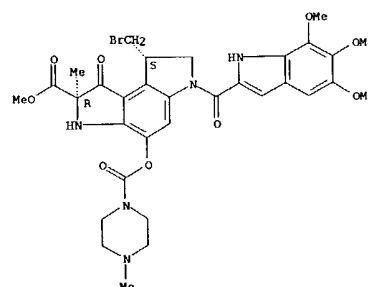
RN 171599-26-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[(4-morpholinylcarbonyl)oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

● HCl

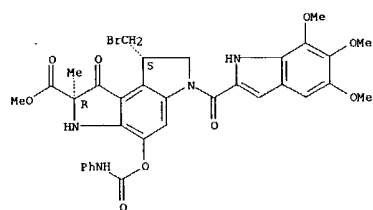
RN 171599-30-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[[[(phenylamino)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 171524-42-8P 171524-43-9P 171599-24-9P

171599-28-3P

RL: SPN (Synthetic preparation); PREP (Preparation)

(synthesis, stability and antitumor activity of duocarmycin

derivs.)

RN 171524-42-8 CAPLUS

CN Glycine, N-[(phenylmethoxycarbonyl)-, 8-(bromomethyl)-1,2,3,6,7,8-

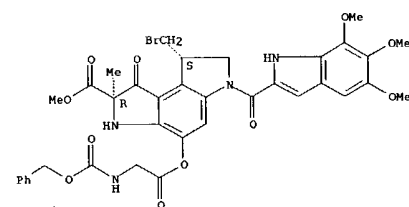
hexahydro-2-(methoxycarbonyl)-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-

2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrole-4-yl ester, (2R-trans)-

(9CI)

(CA INDEX NAME)

Absolute stereochemistry.



RN 171524-43-9 CAPLUS

CN β-Alanine, N-[(phenylmethoxycarbonyl)-, 8-(bromomethyl)-1,2,3,6,7,8-

hexahydro-2-(methoxycarbonyl)-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-

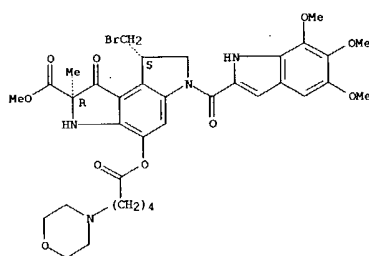
2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrole-4-yl ester, (2R-trans)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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● HCl

RN 171599-28-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-

1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[(1-pyrrolidinylcarbonyl)oxy]-6-

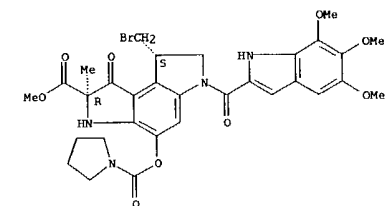
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,

(2R-trans)-

(9CI)

(CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

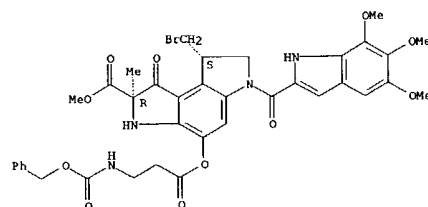
hexahydro-2-(methoxycarbonyl)-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-

2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrole-4-yl ester, (2R-trans)-

(9CI)

(CA INDEX NAME)

Absolute stereochemistry.



RN 171599-24-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-

1,2,3,6,7,8-hexahydro-2-methyl-4-[(5-(4-morpholinyl)-1-oxopentyl)oxy]-6-

[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,

monohydrochloride, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 67 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:741571 CAPLUS

DN 123:285601

TI Duocarmycins, potent antitumor antibiotics produced by Streptomyces

sp.

structures and chemistry

AU Yasuzawa, Tohru; Muroi, Ken'ichi; Ichimura, Michio; Takahashi, Isami;

Ogawa, Tatsuhiro; Takahashi, Keiichi; Sano, Hiroshi; Saitoh, Yutaka

CS Tokyo Res. Lab., Tokyo, 194, Japan

SO Chemical & Pharmaceutical Bulletin (1995), 43(3), 378-91

CODEN: CPBTAL; ISSN: 0009-2363

PB Pharmaceutical Society of Japan

DT Journal

LA English

AB Seven novel potent antitumor antibiotics, duocarmycins A, C1, C2, D,

B1,

B2 and SA, were isolated from three independently collected

Streptomyces

sp. The complete structures, including absolute stereochem., were

determined by spectral and chemical studies of those duocarmycins and several

derivs.

Duocarmycins A and SA possess a

1,2,7,7a-tetrahydrocycloprop[1,2-c]indol-4-

one subunit, a common pharmacophore with that of CC-1065 found from

Streptomyces zelensis.

IT 169102-68-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT (Reactant or reagent)

(isolation and structures of seven duocarmycins, potent antitumor

antibiotics produced by Streptomyces sp.)

RN 169102-68-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-

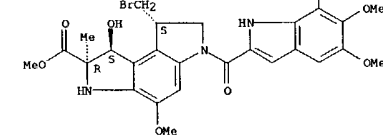
1,2,3,6,7,8-hexahydro-1-hydroxy-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-

indol-2-yl)carbonyl]-, methyl ester, [2R-(2a,3a,4b)]-

(9CI)

(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 129953-21-5P 168776-83-8P 168776-86-1P

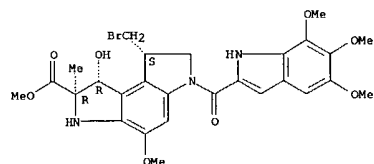
168776-88-3P

10/069,202

L14 ANSWER 67 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (isolation and structures of seven duocarmycins, potent antitumor  
 antibiotics produced by Streptomyces sp.)  
 RN 129953-21-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-

1,2,3,6,7,8-hexahydro-1-hydroxy-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-  
 indol-2-yl)carbonyl]-, methyl ester, [1R-(1a,2B,8a)]-  
 (9CI) (CA INDEX NAME)

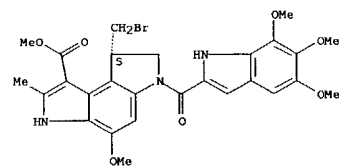
Absolute stereochemistry. Rotation (-).



RN 168776-83-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-

tetrahydro-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]  
 -, methyl ester, (S)- (9CI) (CA INDEX NAME)

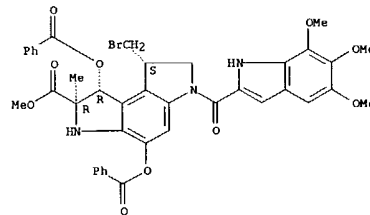
Absolute stereochemistry. Rotation (-).



RN 168776-86-1 CAPLUS

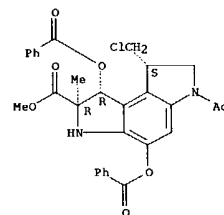
L14 ANSWER 67 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,4-bis(benzoyloxy)-8-  
 (bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-  
 2-yl)carbonyl]-, methyl ester, [1R-(1a,2B,8a)]- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

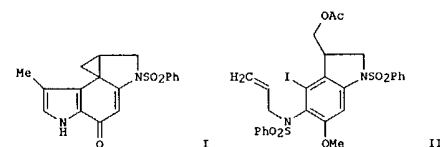


RN 168776-88-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-acetyl-1,4-  
 bis(benzoyloxy)-8-(chloromethyl)-1,2,3,6,7,8-hexahydro-2-methyl-  
 methyl ester, [1R-(1a,2B,8a)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L14 ANSWER 68 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1995:689509 CAPLUS  
 DN 123:111712  
 TI Anticancer agents. 22. Efficient total synthesis of the  
 pharmacophore of  
 the anticancer antibiotic CC-1065 by zirconocene- and  
 palladium-initiated  
 cyclizations  
 AU Tietze, Lutz F.; Buhr, Wilm  
 CS Inst. Org. Chem., Univ. Tammannstrasse, Goettingen, D-37077, Germany  
 SO Angewandte Chemie, International Edition in English (1995), 34(12),  
 1366-8  
 CODEN: ACIEAY; ISSN: 0570-0833  
 PB VCH  
 DT Journal  
 LA English  
 GI



AB The total synthesis of the pharmacophore of CC-1065, I, was achieved  
 via  
 palladium catalyzed cyclization of indole iodide II.

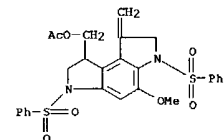
IT 165817-13-0P 165817-15-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

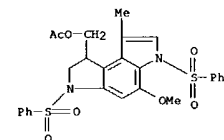
RACT  
 (Reactant or reagent)  
 (total synthesis of pharmacophore of CC-1065 via zirconocene and  
 palladium-catalyzed cyclizations)

RN 165817-13-0 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol,  
 1,2,3,6,7,8-hexahydro-5-methoxy-8-  
 methylene-3,6-bis(phenylsulfonyl)-, acetate (ester) (9CI) (CA INDEX  
 NAME)

L14 ANSWER 68 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 165817-15-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol,  
 1,2,3,6,7,8-hexahydro-5-methoxy-8-  
 methyl-3,6-bis(phenylsulfonyl)-, acetate (ester) (9CI) (CA INDEX  
 NAME)

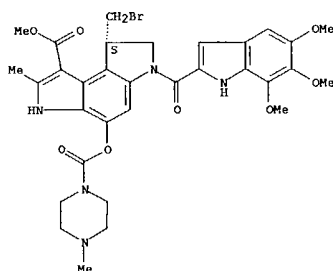


10/069,202

L14 ANSWER 69 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AN 1995:389254 CAPLUS  
 DN 122:177884  
 TI Intracellular carboxyl esterase activity is a determinant of cellular sensitivity to the antineoplastic agent KW-2189 in cell lines resistant to cisplatin and CPT-11  
 AU Ogasawara, Hayato; Nishio, Kazuto; Kanzawa, Fumihiko; Lee, Yong-Sik; Funayama, Yasunori; Ohira, Tatsuo; Kuraishi, Yasunobu; Isogai, Yukihide; Saijo, Nagahiro  
 CS Pharmacology Div., National Cancer Center Res. Inst., Tokyo, 104, Japan  
 SO Japanese Journal of Cancer Research (1995), 86(1), 124-9  
 CODEN: JJCRAP; ISSN: 0910-5050  
 DT Japanese Cancer Association  
 LA English  
 AB KW-2189, a novel antitumor antibiotic belonging to the duocarmycins, possesses marked DNA-binding activity upon activation by carboxyl esterase to its active form, DU-86. Three duocarmycins, KW-2189, DU-86 and duocarmycin SA, were active against the cisplatin (CDDP)-resistant human non-small cell lung cancer cell lines PC-9/CDDP and PC-14/CDDP, and the multidrug-resistant human small cell lung cancer cell line H69/VP. However, HAC2/O.1, a CDDP-resistant human ovarian cancer cell line which is also resistant to CPT-11 because of decreased intracellular activation of CPT-11, was about 12.8-fold more resistant to KW-2189. HAC2/O.1 was not resistant to other duocarmycins as compared to its parental cell line, HAC2. There was no difference between HAC2 and HAC2/O.1 with regard to the intracellular accumulation of KW-2189. Addition of 130 mU/mL of carboxyl esterase to the culture medium did not influence the sensitivity of HAC2 cells to KW-2189. However, the sensitivity of HAC2/O.1 cells to KW-2189 was enhanced to the level of HAC2. These results suggest that HAC2/O.1 is less potent than HAC2 in activating KW-2189. The carboxyl esterase activity of whole-cell and microsomal exts. from HAC2/O.1 was approx. 60% of that from HAC2. The cell-free experiment revealed that KW-2189 bound to DNA more efficiently in the presence of HAC2 than HAC2/O.1 cell extract. It was concluded that decreased intracellular carboxyl esterase activity in

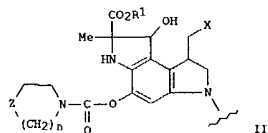
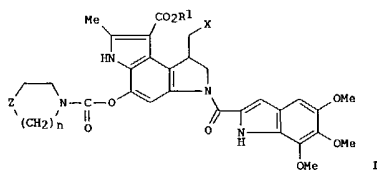
L14 ANSWER 69 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)  
 HAC2/O.1 cells caused decreased intracellular conversion of KW-2189 to its active form, thus producing resistance to KW-2189. The decreased conversion of CPT-11 to SN-38 in HAC2/O.1 cells might be explained by decreased carboxyl esterase activity.  
 IT 154889-68-6, KW-2189  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (intracellular carboxyl esterase activity as determinant of cellular sensitivity to the antineoplastic agent KW-2189 in cell lines resistant to cisplatin and CPT-11)  
 RN 154889-68-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyloxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 70 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AN 1995:347075 CAPLUS  
 DN 122:132847  
 TI Method for preparation of duocarmycin derivatives with antitumor activity  
 IN Kinugawa, Masahiko; Sakaguchi, Akihiko; Ogasa, Takehiro; Saito, Hiromitsu; Nagamura, Akihito; Tomioka, Shinji  
 PA Kyowa Hakko Kogyo Kk, Japan  
 SO Jpn. Kokai Tokkyo Koho, 11 pp.  
 CODEN: JKKXAF  
 DT Patent  
 LA Japanese  
 FAN.CNF 1  

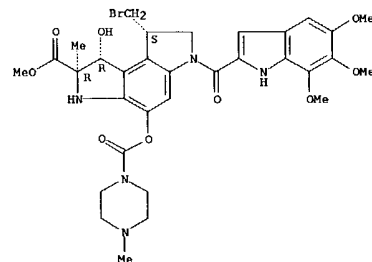
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06298762	A2	19941025	JP 1993-85943	19930413
PRAI JP 1993-85943		19930413		
OS CASREACT 122:132847; MARPAT 122:132847				
GI				



AB The title compds. (I: R1 = lower alkyl, allyl, CH2Ph; X = Cl, Br; Z = CH2, O, NR2; wherein R2 = H, lower alkyl; n = 1-4), useful as antitumor agents (no data), are prepared by treating 1,2,3,4-tetrahydro-3H-pyrrolo[3,2-e]indole-7-carboxylic acid derivative (II; R1, X, Z, n = same as above).

L14 ANSWER 70 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)  
 Thus, Me (15,7R)-1-bromomethyl-7-methyl-5-[(4-methylpiperazinyl)carbonyloxy]-8-oxo-3-[(5,6,7-trimethoxyindol-2-yl)carbonyl]-1,2,7,8-tetrahydro-3H-pyrrolo[3,2-e]indole-7-carboxylate was reduced by NaBH4 in allyl alc. to give, after silica gel chromatog., intermediate II (R1 = Me, X = Br, Z = MeN, n = 2). The latter compd. was stirred with MeSO3H in CH2Cl2 at 47-53° for 5 h to give 86.3% title compd. I (R1 = Me, X = Br, Z = MeN, n = 2).  
 IT 160819-29-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and dehydration in preparation of duocarmycin derivs. with antitumor activity)  
 RN 160819-29-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyloxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R,2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



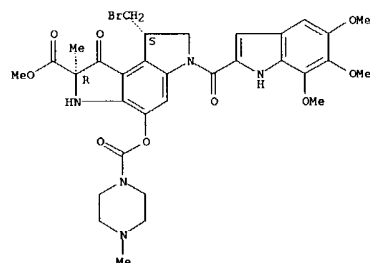
IT 154901-65-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and reduction with sodium borohydride in preparation of duocarmycin derivs. with antitumor activity)  
 RN 154901-65-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-

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L14 ANSWER 70 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

1,2,3,6,7,8-hexahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 154889-68-6P 160819-28-3P

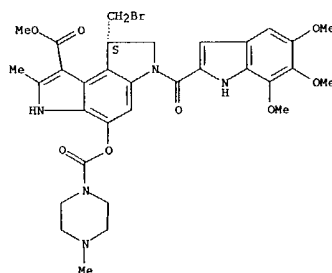
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of duocarmycin derivs. with antitumor activity by acid-catalyzed dehydration of hydroxytetrahydropyrroloindolecarboxylic acid derivative)

RN 154889-68-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 70 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



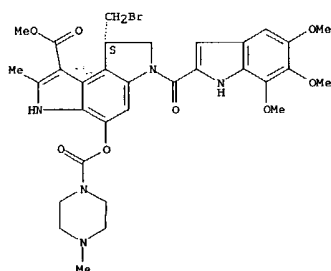
RN 160819-28-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 70 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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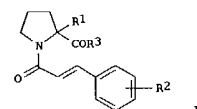


● HBr

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L14 ANSWER 71 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

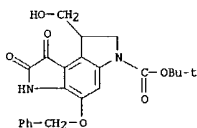
AN 1995:315828 CAPLUS  
DN 122:82075  
TI N-cinnamoylproline derivatives or alkali metal salts as resolving agents for racemates  
IN Terajima, Atsuro; Fukuda, Yasumichi  
PA Kyorin Seiyaku Kk, Japan; Sagami Chem Res  
SO Jpn. Kokai Tokkyo Koho, 4 pp.  
CODEN: JKXAXF  
DT Patent  
LA Japanese  
FAN.CMT 1  
PATENT NO. KIND DATE APPLICATION NO. DATE  
PI JP 06293733 A2 19941021 JP 1992-55536 19920313  
JP 3181671 B2 20010703  
PRAI JP 1992-55536 19920313  
OS MARPAT 122:82075  
GI



AB N-cinnamoylproline derivs. [1: R1 = H, lower alkyl; R2 = H, halo, OH, NO2, lower alkoxy, lower alkyl, (un)substituted Ph; R3 = OH, residue of a reactive group] or alkali metal salts thereof are used as resolving agents of racemates which are difficult to resolve them by conventional resolving agents. Thus, 5-benzyloxy-3-(tert-butoxycarbonyl)-1-hydroxymethyl-7,8-dioxo-1,2,3,6,7,8-hexahydropyrrolo[3,2-e]indole was condensed with N-cinnamoyl-L-proline in the presence of DCC and 4-dimethylaminopyridine in CH2Cl2 at room temperature to give a mixture of diastereomer esters which was separated by silica gel chromatog. to give 152 mg 5-Benzyloxy-3-(tert-butoxycarbonyl)-(1S)-(N-cinnamoyl-L-prolyloxymethyl)-7,8-dioxo-1,2,3,6,7,8-hexahydropyrrolo[3,2-e]indole and 119 mg (1R,S)-diastereomer.  
IT 143874-46-8  
RL: RCT (Reactant); RACT (Reactant or reagent) (optical resolution of (hydroxymethyl)hexahydropyrroloindole derivative by diastereomer ester formation with N-cinnamoyl-L-proline and silica gel

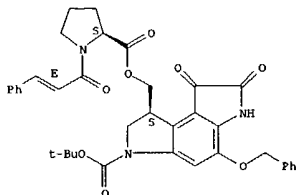
10/069,202

L14 ANSWER 71 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 chromatog.)  
 RN 143874-46-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
 1,6,7,8-tetrahydro-1-  
 (hydroxymethyl)-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester  
 (9CI) (CA INDEX NAME)



IT 149365-69-5P 149365-70-8P  
 RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP  
 (Preparation)  
 (optical resolution of (hydroxymethyl)hexahydropyrroloindole  
 derivative by  
 diastereomer ester formation with N-cinnamoyl-L-proline and silica  
 gel  
 chromatog.)  
 RN 149365-69-5 CAPLUS  
 CN L-Proline, 1-(1-oxo-3-phenyl-2-propenyl)-, [3-[(1,1-  
 dimethylethoxy)carbonyl]-1,2,3,6,7,8-hexahydro-7,8-dioxo-5-  
 (phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (S)-  
 (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.

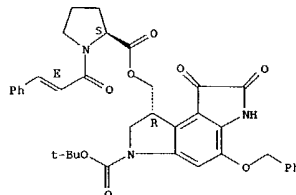


L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1994:605331 CAPLUS  
 DN 121:205331  
 TI preparation of (trifluoromethyl)pyrroloindolecarboxylic esters as  
 antitumor agents  
 IN Terashima, Shiro; Fukuda, Yasumichi; Oomori, Yasuo  
 PA Kyorin Pharmaceutical Co., Ltd., Japan; Sagami Chemical Research  
 Center  
 SO PCT Int. Appl., 124 pp.  
 CODEN: PIKXKD  
 DT Patent  
 LA Japanese  
 FAN. CNT 1  

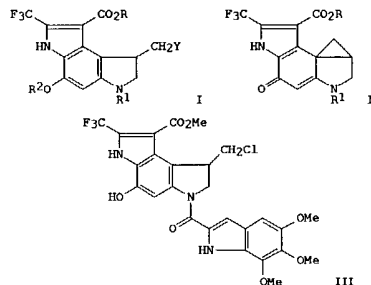
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9404535	A1	19940303	WO 1993-JP1159	19930819
W: AU, BB, BG, BR, CA, CZ, FI, HU, KR, LK, MG, MN, MW, NO, NZ,				
RO, RU, SD, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT,				
SE, BF, BJ, CF, CG, CI, CM, GA, GM, ML, MR, NE, SN, TD, TG				
JP 06116269	A2	19940426	JP 1993-204255	19930818
JP 3514490	B2	20040331		
EP 656360	A1	19950607	EP 1994-908108	19930819
EP 656360	B1	20021120		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT,				
HU 71493	A2	19951128	HU 1995-494	19930819
AU 689443	B2	19980402	AU 1993-47618	19930819
AU 9347618	A1	19940315		
CA 2142869	C	20020101	CA 1993-2142869	19930819
AT 228132	E	20021215	AT 1994-908108	19930819
PT 656360	T	20030228	PT 1994-908108	19930819
ES 2188608	T3	20030701	ES 1994-908108	19930819
TW 394774	B	20000621	TW 1993-82108171	19931004
US 5629430	A	19970513	US 1995-381981	19950614
PRAI JP 1993-222862	A	19930818		
JP 1993-204255	A	19930818		
WO 1993-JP1159	W	19930819		
OS MARPAT 121:205331				
GI				

L14 ANSWER 71 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 RN 149365-70-8 CAPLUS  
 CN L-Proline, 1-(1-oxo-3-phenyl-2-propenyl)-, [3-[(1,1-  
 dimethylethoxy)carbonyl]-1,2,3,6,7,8-hexahydro-7,8-dioxo-5-  
 (phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (R)-  
 (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



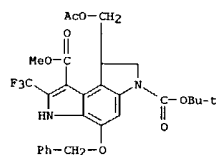
L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



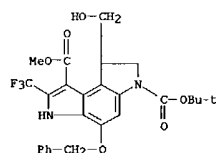
AB The title compds. [I, II; R = alkyl; R1 =  $\alpha$ -amino acid residue,  
 etc.; R2 = H, protecting group; Y = halo, arylsulfonyl, etc.] are  
 prepared I (R = Me, R1 = Me3CO2C, R2 = H, Y = Cl) was added to 3M  
 HCl-EtOAc  
 with stirring at room temperature, the residue after distillation was  
 treated with  
 5,6,7-trimethoxyindole-2-carboxylic acid and  
 1-(3-dimethylaminopropyl)-3-  
 ethylcarbodiimide HCl in DMF with stirring at room temperature under  
 Ar to give  
 824 III, which showed IC50 of 0.24 ng/mL against P-388 mouse leukemic  
 cells. Also prepared and tested were 103 addnl. I and II.  
 IT 194093-62-4P 194093-63-5P 194093-64-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT  
 (Reactant or reagent)  
 (preparation and reaction of, in preparation of antitumor agents)  
 RN 194093-62-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-,  
 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)

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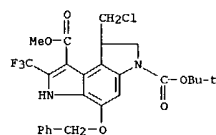
L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 194093-63-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)

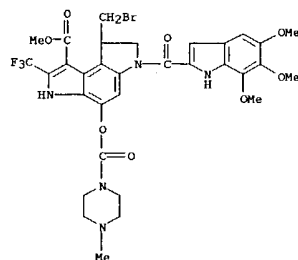


RN 194093-64-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)

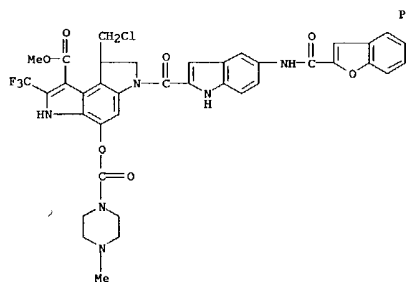


IT 157823-03-5P 157823-04-6P 157823-05-7P

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 157823-05-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



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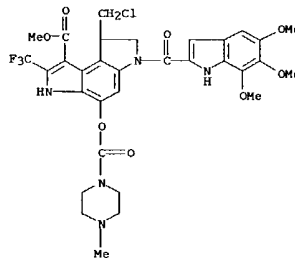
L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

157823-06-8P 157823-08-0P 157823-09-1P  
157823-10-4P 157823-11-5P 157823-12-6P  
157823-40-0P 157823-41-1P 157823-42-2P  
157823-43-3P 157823-44-4P 157823-45-5P  
157823-46-6P 157823-47-7P 157823-48-8P  
157823-49-9P 157823-50-2P 157823-51-3P  
157823-52-4P 157823-53-5P 157823-54-6P  
157823-56-8P 157904-26-2P 157904-27-3P  
157904-34-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of, as antitumor agent)

RN 157823-03-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-2-(trifluoromethyl)-6-[[5,6,7-trimethoxy-1H-indol-2-yl]carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 157823-04-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

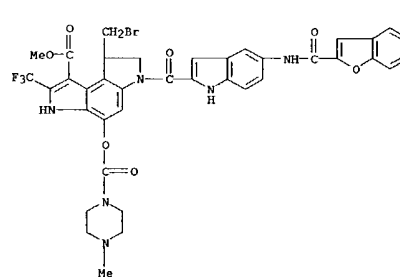
tetrahydro-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-2-(trifluoromethyl)-6-[[5,6,7-trimethoxy-1H-indol-2-yl]carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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● HCl

RN 157823-06-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



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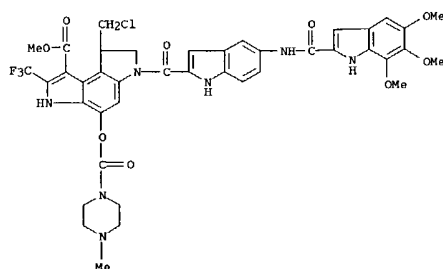
● HCl

RN 157823-08-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

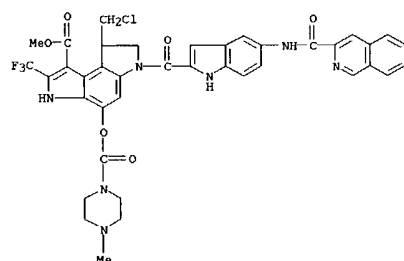
tetrahydro-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-2-(trifluoromethyl)-6-[[5-[[5,6,7-trimethoxy-1H-indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

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L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

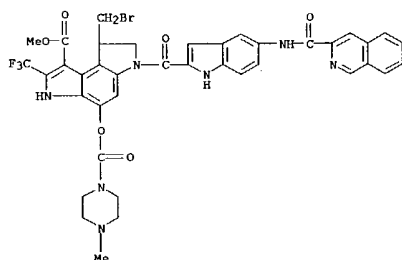


RN 157823-09-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-6-[[5-[(3-isoquinolylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-  
4-[[4-methyl-1-piperazinyl]carbonyloxy]-2-(trifluoromethyl)-,  
methyl  
ester (9CI) (CA INDEX NAME)



L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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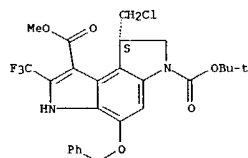


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● HCl

RN 157823-12-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-,  
6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

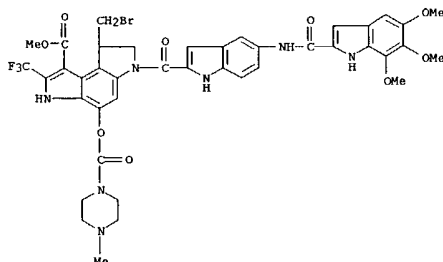
Absolute stereochemistry. Rotation (-).



RN 157823-40-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-4-[[4-methyl-1-piperazinyl]carbonyloxy]-2-(trifluoromethyl)-6-  
-  
[[5,6,7-trimethoxy-2-benzofuranyl]carbonyl]-, methyl ester,

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 157823-10-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-4-[[4-methyl-1-piperazinyl]carbonyloxy]-2-(trifluoromethyl)-6-  
-  
[[5-[[5,6,7-trimethoxy-1H-indol-2-yl]carbonyl]amino]-1H-indol-2-  
yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

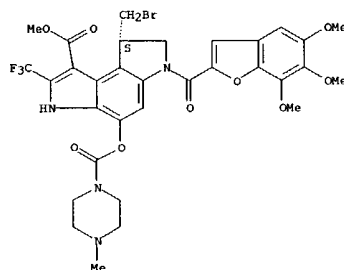


RN 157823-11-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-6-[[5-[(3-isoquinolylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-  
4-[[4-methyl-1-piperazinyl]carbonyloxy]-2-(trifluoromethyl)-, methyl  
ester, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.

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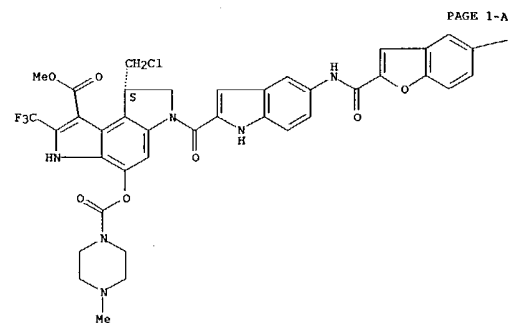
● HCl

RN 157823-41-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-6-[[5-[[5-methoxy-2-benzofuranyl]carbonyl]amino]-1H-indol-2-  
yl]carbonyl]-4-[[4-methyl-1-piperazinyl]carbonyloxy]-2-(trifluoromethyl)-  
-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

10/069,202

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



OMe

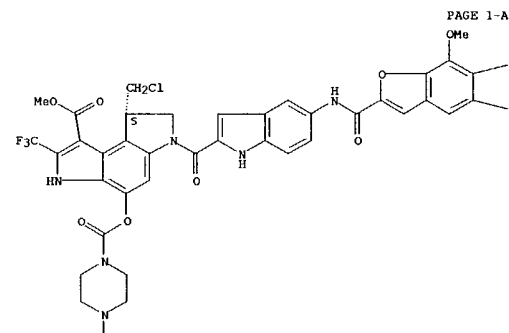
PAGE 1-B

● HCl

RN 157823-42-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-6-[[5-[[6-methoxy-2-benzofuranyl]carbonyl]amino]-1H-indol-2-  
yl]carbonyl]-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-2-(trifluoromethyl)-

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
6-[[5-[[[5,6,7-trimethoxy-2-benzofuranyl]carbonyl]amino]-1H-indol-2-  
yl]carbonyl]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA  
INDEX  
NAME)

Absolute stereochemistry. Rotation (+).



OMe

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OMe

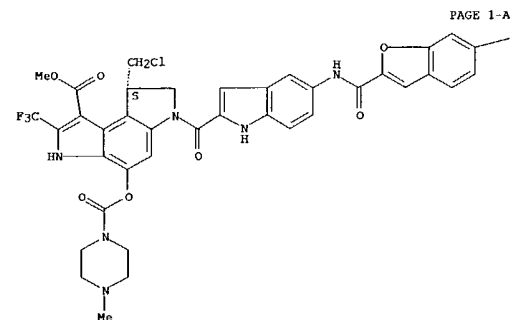
PAGE 2-A

Me

● HCl

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OMe

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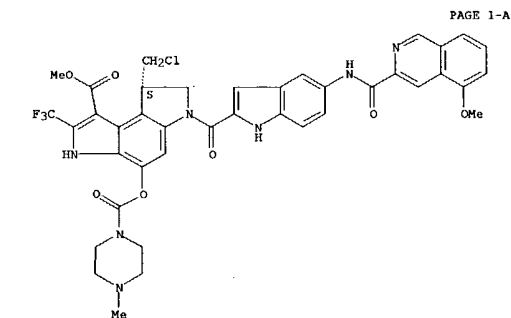
● HCl

RN 157823-43-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-  
tetrahydro-6-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-2-(trifluoromethyl)-

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
RN 157823-44-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-

tetrahydro-6-[[5-[[[5-methoxy-3-isoquinoliny]carbonyl]amino]-1H-indol-2-  
yl]carbonyl]-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-2-(trifluoromethyl)-  
, methyl ester, monohydrochloride, (5)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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● HCl

RN 157823-45-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-

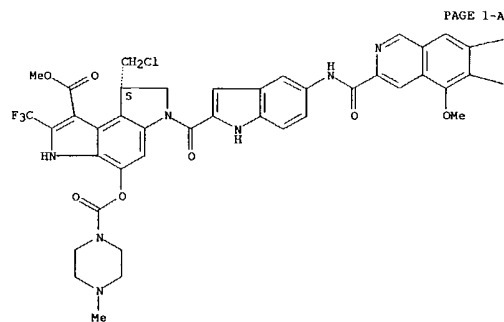
tetrahydro-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-2-(trifluoromethyl)-6-  
[[5-[[[5,6,7-trimethoxy-3-isoquinoliny]carbonyl]amino]-1H-indol-2-  
yl]carbonyl]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX  
NAME)

Absolute stereochemistry. Rotation (+).



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L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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OMe

OMe

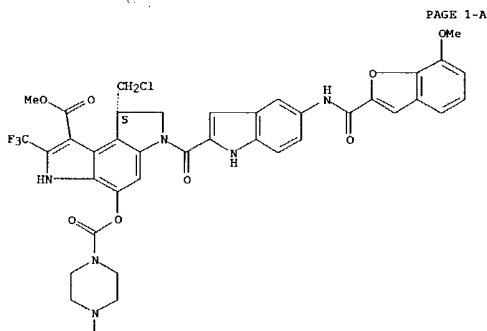
● HCl

RN 157823-46-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-

tetrahydro-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[[5-[[9H-pyrido[3,4-  
b]indol-3-ylcarbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-,

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
yl]carbonyl]-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-  
-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



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Me

RN 157823-48-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-

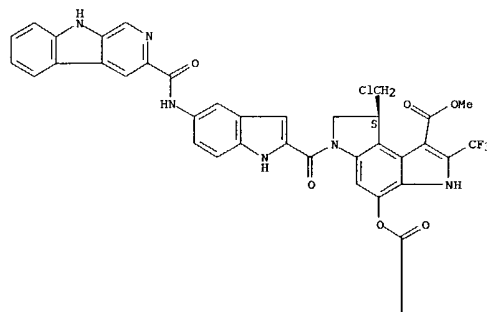
tetrahydro-4-[[[4-(2-hydroxyethyl)-1-piperazinyl]carbonyl]oxy]-6-[[5-[[7-  
methoxy-2-benzofuranyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-  
(trifluoromethyl)-, methyl ester, monohydrochloride, (S)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.

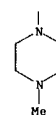
L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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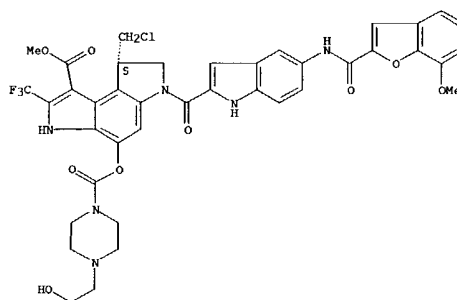
● HCl

RN 157823-47-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-

tetrahydro-6-[[5-[[7-methoxy-2-benzofuranyl]carbonyl]amino]-1H-indol-2-

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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● HCl

RN 157823-49-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-

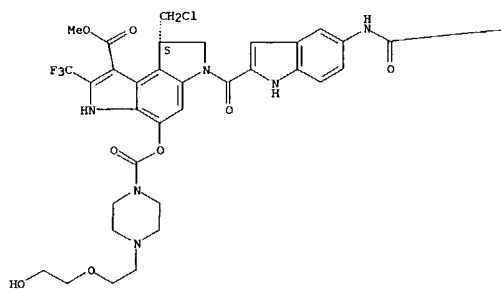
tetrahydro-4-[[[4-[2-(2-hydroxyethoxy)ethyl]-1-piperazinyl]carbonyl]oxy]-6-  
[[5-[[7-methoxy-2-benzofuranyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-  
(trifluoromethyl)-, methyl ester, monohydrochloride, (S)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.

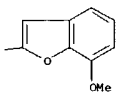
10/069,202

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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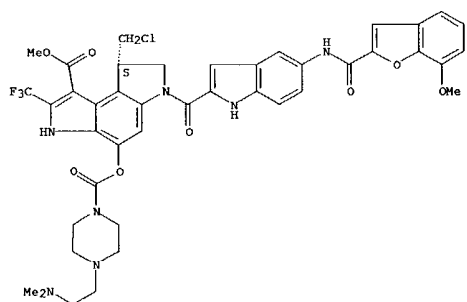
● HCl

RN 157823-50-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
4-[[[1,4'-bipiperidin]-1'-ylcarbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[5-[[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-,

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
(trifluoromethyl)-, methyl ester, dihydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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●2 HCl

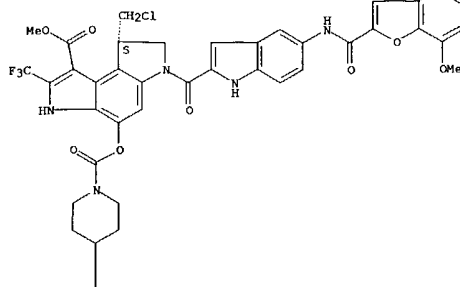
RN 157823-52-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
4-[[[4-(2-aminoethyl)-1-piperazinyl]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[5-[[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, dihydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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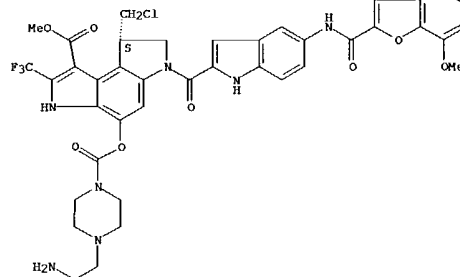


● HCl

RN 157823-51-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[4-(2-(dimethylamino)ethyl)-1-piperazinyl]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[[5-[[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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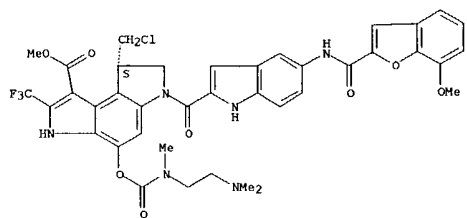
●2 HCl

RN 157823-53-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-4-[[[2-(dimethylamino)ethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[[5-[[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/069,202

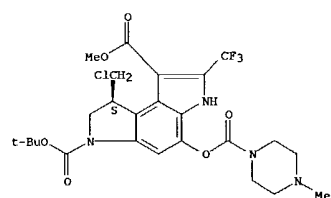
L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



● HCl

RN 157823-54-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
8-(chloromethyl)-7,8-dihydro-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI)  
(CA INDEX NAME)

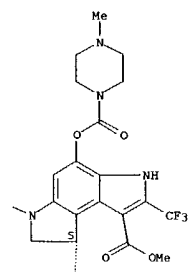
Absolute stereochemistry.



RN 157823-56-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
6,6'-[carbonylbis(imino-1H-indole-5,2-diylcarbonyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[4-

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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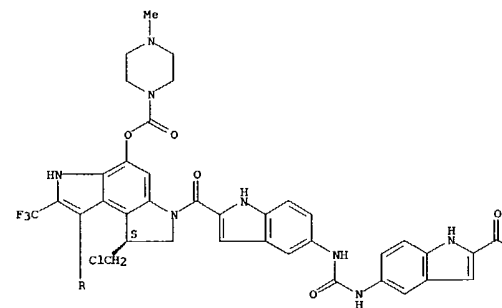
PAGE 2-B

RN 157904-26-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)  
Absolute stereochemistry. Rotation (-).

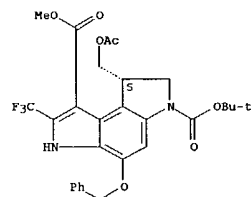
L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
methyl-1-piperazinyl]carbonyl]oxy]-2-(trifluoromethyl)-, dimethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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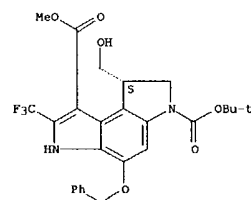


L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 157904-27-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

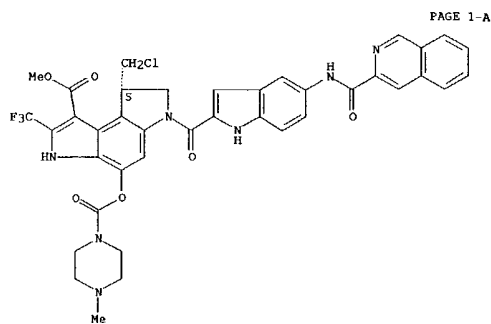


RN 157904-34-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[[5-[(3-isquinolinylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

10/069,202

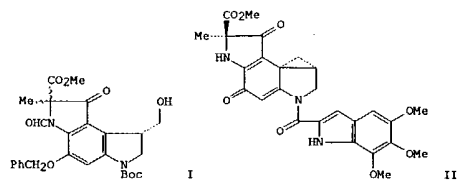
L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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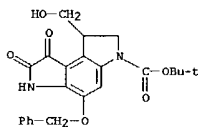
● HCl

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1994:557348 CAPLUS  
 DN 121:157348  
 TI Synthetic studies on duocarmycin. 2. Synthesis and cytotoxicity of natural  
 (+)-duocarmycin A and its three possible stereoisomers  
 AU Fukuda, Yasumichi; Nakatani, Kazuhiko; Terasima, Shiro  
 CS Cent. Res. Lab., Kyorin Pharm. Co., Ltd., Tochigi, 329-01, Japan  
 SO Tetrahedron (1994), 50(9), 2809-20  
 CODEN: TETRA8; ISSN: 0040-4020  
 DT Journal  
 LA English  
 GI



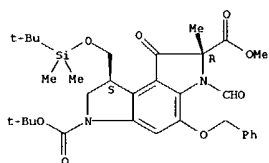
AB The title synthesis was achieved by featuring the optical resolution of two types of the tricyclic intermediates, e.g., I, and the synthetic scheme established in the synthesis of racemic compds. In vitro cytotoxicity assay against P388 murine leukemia obviously showed that the absolute configuration of cyclopropane moiety in (+)-duocarmycin A (II) is closely related to its cytotoxicity.  
 IT 143874-46-8  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (condensation of, with cinnamoylproline)  
 RN 143874-46-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6,7,8-tetrahydro-1-(hydroxymethyl)-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 132628-67-2 132628-68-3  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (desilylation of)  
 RN 132628-67-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[1,1-dimethylethyl]dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, trans- (9CI) (CA INDEX NAME)

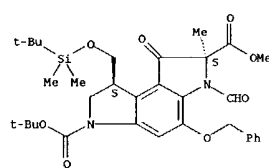
Relative stereochemistry.



RN 132628-68-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[1,1-dimethylethyl]dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, cis- (9CI) (CA INDEX NAME)

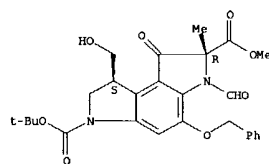
Relative stereochemistry.

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 149365-66-2P 149365-67-3P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and condensation of, with acetylmandelic acid)  
 RN 149365-66-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 3-formyl-2,3,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

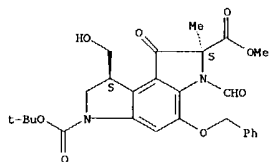


RN 149365-67-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3,7(2H)-dicarboxylic acid, 6-formyl-1,6,7,8-tetrahydro-1-(hydroxymethyl)-7-methyl-8-oxo-5-(phenylmethoxy)-, 3-(1,1-dimethylethyl) 7-methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

10/069,202

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 157478-14-3P 157478-15-4P 157478-16-5P  
157478-17-6P

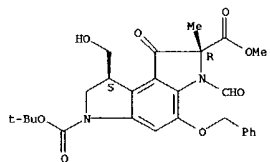
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and conversion of, to  
(indolylcarbonyl)benzodipyrrolecarboxylat  
e)

RN 157478-14-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,  
3-formyl-2,3,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-  
(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (2R-trans)-  
(9CI)

(CA INDEX NAME)

Absolute stereochemistry.



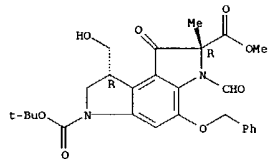
RN 157478-15-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,  
3-formyl-2,3,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-  
(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (2S-trans)-  
(9CI)

(CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 149365-69-5P

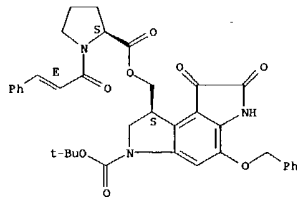
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and conversion of, to ester)

RN 149365-69-5 CAPLUS

CN L-Proline, 1-((1-oxo-3-phenyl-2-propenyl)-, [3-[(1,1-  
dimethylethoxy)carbonyl]-1,2,3,6,7,8-hexahydro-7,8-dioxo-5-  
(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl)methyl ester, (S)-  
(9CI)

(CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



IT 157478-20-1P 157478-21-2P 157478-22-3P  
157478-23-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT

(Reactant or reagent)

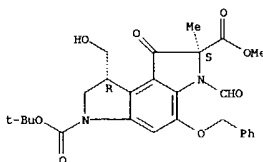
(preparation and debenzoylation of)

RN 157478-20-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
1,2,3,6,7,8-hexahydro-2-

methyl-8-[[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI)  
(CA

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

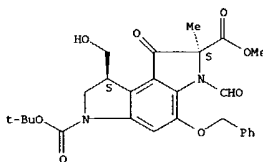


RN 157478-16-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,  
3-formyl-2,3,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-  
(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (2S-cis)-  
(9CI)

(CA INDEX NAME)

Absolute stereochemistry.



RN 157478-17-6 CAPLUS

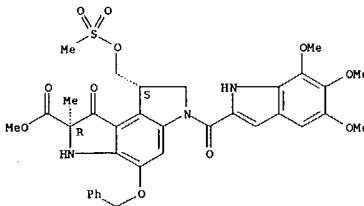
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,  
3-formyl-2,3,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-  
(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (2R-cis)-  
(9CI)

(CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
INDEX NAME

Absolute stereochemistry. Rotation (+).



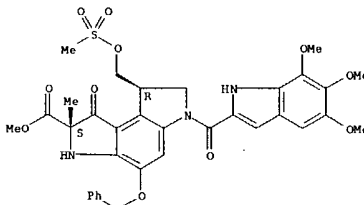
RN 157478-21-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
1,2,3,6,7,8-hexahydro-2-

methyl-8-[[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2S-trans)- (9CI)

(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



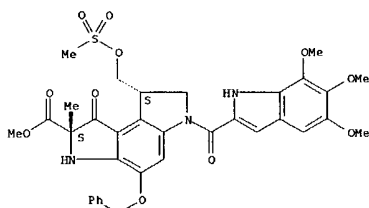
RN 157478-22-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
1,2,3,6,7,8-hexahydro-2-

methyl-8-[[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2S-cis)- (9CI)  
(CA

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
INDEX NAME

Absolute stereochemistry. Rotation (-).

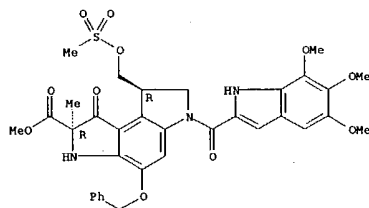


RN 157478-23-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
1,2,3,6,7,8-hexahydro-2-

methyl 8-[[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]]-, methyl ester, (2R-cis)- (9CI)

(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 157478-33-6P 157478-34-7P

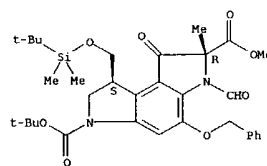
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
(Reactant or reagent)

(prepn. and desilylation of)

RN 157478-33-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,  
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)-2-methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

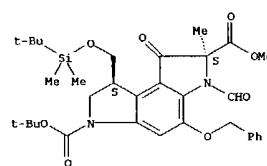
Absolute stereochemistry. Rotation (+).



RN 157478-34-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,  
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)-2-methyl ester, (2S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 149365-68-4P 149405-52-7P 149405-56-1P

149405-57-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT  
(Reactant or reagent)  
(preparation and hydrolysis of)

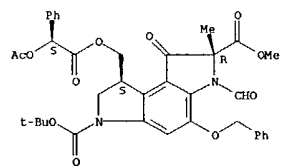
L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 149365-68-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,

8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)-2-methyl ester, [2R-[2α,8β(5\*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

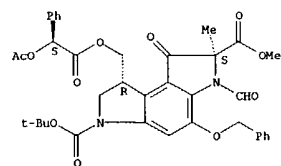


RN 149405-52-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,

8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 6-(1,1-dimethylethyl) ester, [2S-[2α,8β(R\*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



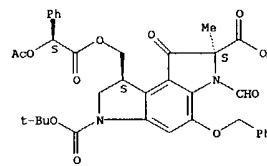
RN 149405-56-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,

8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 6-(1,1-dimethylethyl) ester, [2S-[2α,8α(R\*)]]- (9CI) (CA INDEX NAME)

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry. Rotation (-).

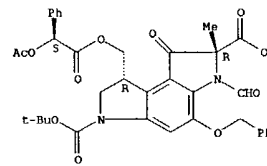


RN 149405-57-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,

8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 6-(1,1-dimethylethyl) ester, [2R-[2α,8α(5\*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 149405-53-8P 149405-54-9P 157478-18-7P

157478-19-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT  
(Reactant or reagent)  
(preparation and mesylation of)

RN 149405-53-8 CAPLUS

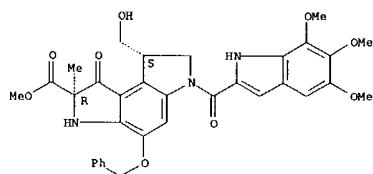
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
1,2,3,6,7,8-hexahydro-8-

(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

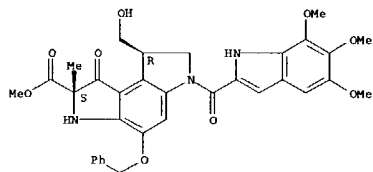
10/069,202

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 149405-54-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
1,2,3,6,7,8-hexahydro-8-  
(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2S-trans)- (9CI) (CA INDEX NAME)

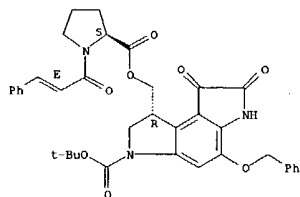
Absolute stereochemistry. Rotation (-).



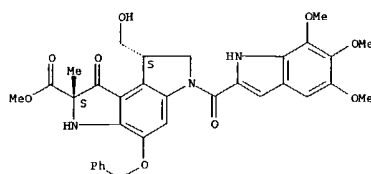
RN 157478-18-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
1,2,3,6,7,8-hexahydro-8-  
(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

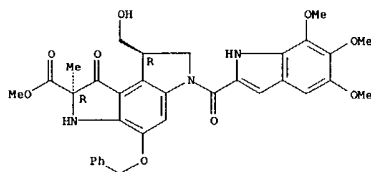


L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 157478-19-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
1,2,3,6,7,8-hexahydro-8-  
(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

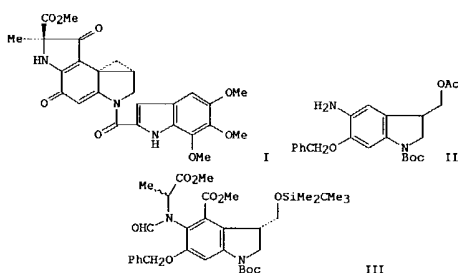


IT 149365-70-8P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)  
RN 149365-70-8 CAPLUS  
CN L-Proline, 1-[(1-oxo-3-phenyl-2-propenyl)-, [3-[(1,1-dimethylethoxy)carbonyl]-1,2,3,6,7,8-hexahydro-7,8-dioxo-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrole-1-yl]methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

L14 ANSWER 74 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:557347 CAPLUS  
DN 121:157347  
TI Synthetic studies on duocarmycin. 1. Total synthesis of  
dl-duocarmycin A  
and its 2-epimer  
AU Fukuda, Yasumichi; Itoh, Yoshio; Nakatani, Kazuhiko; Terashima, Shiro  
C5 Sagami Chem. Res. Cent., Kanagawa, 229, Japan  
SO Tetrahedron (1994), 50(9), 2793-808  
CODEN: TETRA; ISSN: 0040-4020  
DT Journal  
LA English  
OS CASREACT 121:157347  
GI



AB The title synthesis of dl-duocarmycin A (I) and its 2-epimer was first achieved by employing novel methoxycarbonylation of the C4-position of the 5-aminoindoline II by way of the isatin and subsequent Dieckmann cyclization of indolecarboxylate III to the Me 2-methylindoxyl-2-carboxylate as key steps. In vitro cytotoxicity assay against P388 murine leukemia obviously disclosed that cytotoxicities of the synthesized compds. are comparable and almost half of that of natural (+)-duocarmycin A.

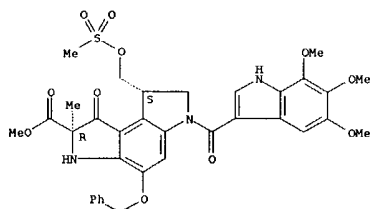
IT 157485-12-6P 157485-13-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT (Reactant or reagent)  
(preparation and hydrogenation of)  
RN 157485-12-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
1,2,3,6,7,8-hexahydro-2-

10/069,202

L14 ANSWER 74 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

methyl-8-[[[(methylsulfonyl)oxy)methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-3-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

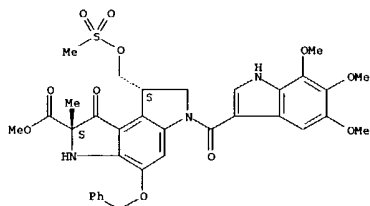
Relative stereochemistry.



RN 157485-13-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-

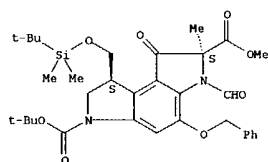
methyl-8-[[[(methylsulfonyl)oxy)methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-3-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L14 ANSWER 74 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy)methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

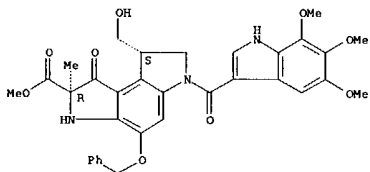


IT 157485-10-4P 157485-11-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT (Reactant or reagent)

(preparation and mesylation of)  
RN 157485-10-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-

(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-3-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 157485-11-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-

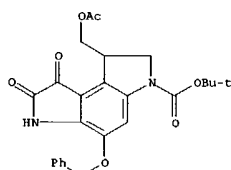
(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-3-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L14 ANSWER 74 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

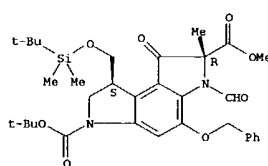
IT 132628-62-7P 132628-67-2P 132628-68-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT (Reactant or reagent)  
(preparation and hydrolysis of)  
RN 132628-62-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[(acetyloxy)methyl]-1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



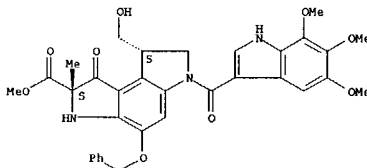
RN 132628-67-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy)methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



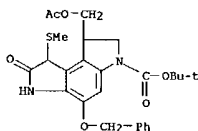
RN 132628-68-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,

L14 ANSWER 74 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

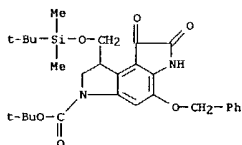


IT 132628-61-6P 132628-63-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT (Reactant or reagent)  
(preparation and oxidation of)  
RN 132628-61-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[(acetyloxy)methyl]-1,6,7,8-tetrahydro-8-(methylthio)-7-oxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 132628-63-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy)methyl]-1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)





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L14 ANSWER 74 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT 143874-46-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

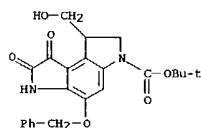
RACT (Reactant or reagent)

(preparation and silylation of)

RN 143874-46-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,

1,6,7,8-tetrahydro-1-(hydroxymethyl)-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 75 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); THU (Therapeutic use); BIOL (Biological

study); USES

(Uses)

(neoplasm inhibition by, DNA damage as mechanism of, activation in relation to)

RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,

8-(bromomethyl)-3,6,7,8-

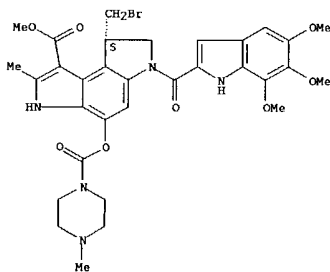
tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-

trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX

NAME)

Absolute stereochemistry.



L14 ANSWER 75 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:548428 CAPLUS

DN 121:148428

TI A novel antitumor antibiotic, KW-2189, is activated by carboxyl

esterase

and induces DNA strand breaks in human small cell lung cancer cells

AU Ogasawara, Hayato; Nishio, Kazuto; Takeda, Yuichiro; Ohmori, Tohru;

Kubota, Naohiro; Funayama, Yasunori; Ohira, Tatsuo; Kuraishi,

Yasunobu

Isogai, Yukihiro; Saijo, Nagahiro

CS Pharmacol. Div., Natl. Cancer Center Res. Inst., Tokyo, 104, Japan

SO Japanese Journal of Cancer Research (1994), 85(4), 418-25

CODEN: JJCREP; ISSN: 0910-5050

DT Journal

LA English

AB The purpose of this study was to examine the DNA-binding potency and

the

mechanisms of cytotoxicity of KW-2189. In order to analyze the

DNA-binding activity of KW-2189, plasmid pBR322 was treated with

KW-2189

with or without pretreatment with carboxyl esterase, and the products

were

examined by agarose gel electrophoresis and restriction enzyme anal.

Cytotoxic activity was examined by exposing a human small-cell lung

cancer

cell line, NCI-H69, to KW-2189 with or without carboxyl esterase.

Alkaline

elution was performed to examine whether KW-2189 induces DNA strand

breaks. DNA treated with KW-2189 and carboxyl esterase migrated

faster

than DNA treated with KW-2189 alone, which migrated at the same rate

as

untreated DNA. In addition DNA treated with esterase-activated

KW-2189 was

protected from digestion by some restriction enzymes. KW-2189 had

concentration-

and time-dependent growth inhibitory effects, with IC50 values from

50 nM

(96 h) to 1900 nM (1 h) in H69 cells. The IC50 values for 4-h

exposure of

H69 to KW-2189 plus 0, 26, 130, and 650 nM carboxyl esterase/mL were

460,

120, 30, and 7 nM, resp. Time-dependent enhancement of cytotoxicity

by

carboxyl esterase was also observed KW-2189 induced DNA strand

breaks in H69

cells in a concentration-dependent manner around the IC50 value.

Apparently: (1)

KW-2189 is activated by carboxyl esterase to its active form(s); (2)

activated KW-2189 has a stronger DNA-binding activity and cytotoxicity

than KW-2189 alone; (3) DNA cleavage is one of the major mechanisms of

KW-2189-mediated cytotoxicity.

IT 154889-68-6, KW 2189

L14 ANSWER 76 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:508766 CAPLUS

DN 121:108766

TI Preparation of tetrahydropyrroloindoles as antitumor agents

IN Terajima, Atsuro; Fukuda, Yasumichi; Oomori, Yasuo

PA Kyorin Seiyaku Kk, Japan; Sagami Chem Res

SO Jpn. Kokai Tokyo Koho, 21 pp.

CODEN: JKKXAF

DT Patent

LA Japanese

FAN.CNT 1

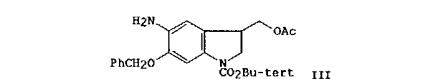
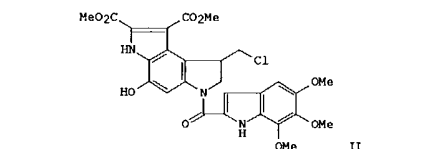
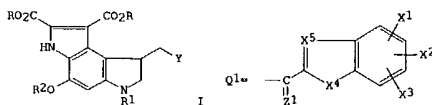
PATENT NO. KIND DATE APPLICATION NO. DATE

PI JP 06122684 A2 19940506 JP 1992-274282 19921013

PRAI JP 1992-274282 19921013

OS MARPAT 121:108766

GI



AB The title compds., e. g., I [R = alkyl; R1 = Q1, etc.; X4 = O, S, NH;

X5 =

CH, N; X1 - X3 = H, OH, etc.; Z1 = O, S, etc.; R2 = H, OH-protecting

group, etc.; Y = halo, etc.] are prepared The title compound II was

prepared in multiple steps from indoline derivative III. II in vitro showed IC50

of 0.31

ng/mL against P388 mouse leukemic cells.

IT 156905-81-6P 156905-82-7P 156905-83-8P

10/069,202

L14 ANSWER 76 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

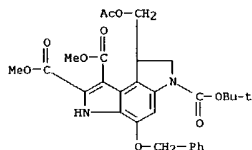
RACT

(Reactant or reagent)

(prepn. and reaction of, in prepn. of antitumor agent)

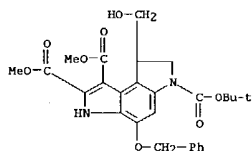
RN 156905-81-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1,2-dimethyl ester (9CI) (CA INDEX NAME)



RN 156905-82-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1,2-dimethyl ester (9CI) (CA INDEX NAME)



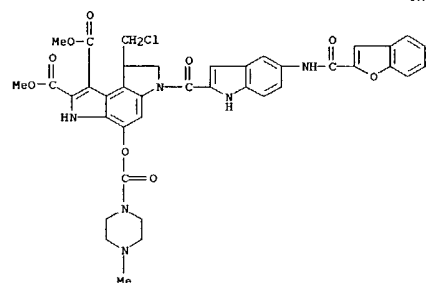
RN 156905-83-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1,2-dimethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 76 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 156905-77-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-, 3,6,7,8-tetrahydro-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



PAGE 1-A

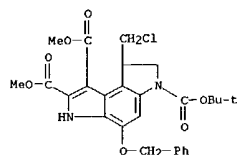
PAGE 2-A

● HCl

RN 156905-78-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(bromomethyl)-, 3,6,7,8-tetrahydro-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, dimethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 76 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 156905-76-9P 156905-77-0P 156905-78-1P

156905-79-2P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic

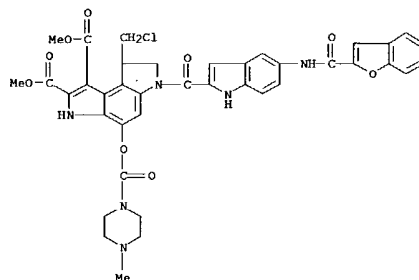
use);

BIOL (Biological study); PREP (Preparation); USES (Uses)

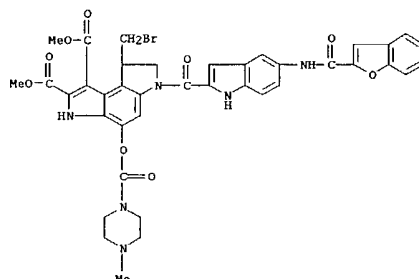
(preparation of, as antitumor agent)

RN 156905-76-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-, 3,6,7,8-tetrahydro-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, dimethyl ester (9CI) (CA INDEX NAME)



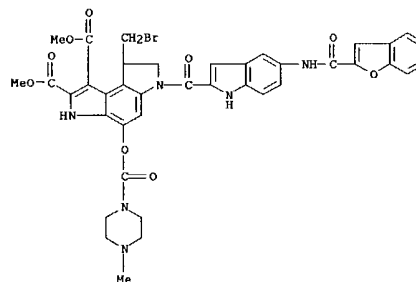
L14 ANSWER 76 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 156905-79-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(bromomethyl)-, 3,6,7,8-tetrahydro-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



10/069,202

L14 ANSWER 76 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)

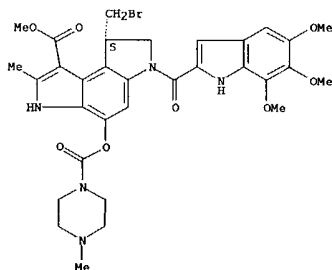
PAGE 2-A

● HCl

L14 ANSWER 77 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)

compd. was deacetylated with K<sub>2</sub>CO<sub>3</sub> in MeOH and chlorinated by CCl<sub>4</sub> and PPh<sub>3</sub> in CH<sub>2</sub>Cl<sub>2</sub> at room temp. to give (3S)-I (R<sub>3</sub> = PhCH<sub>2</sub>, R<sub>4</sub> = Me<sub>3</sub>CO<sub>2</sub>C, X<sub>1</sub> = Cl) which was converted into (S)-KW-2189 II in 5 steps.  
IT 156395-56-1, KW 2189  
RL: RCT (Reactant); RACT (Reactant or reagent) (intermediates for, tetrahydropyrroloindole derivs. as)  
RN 156395-56-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-A

PAGE 2-A

● HCl

IT 156295-27-1P 156295-32-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT (Reactant or reagent) (preparation and chlorination of, by carbon tetrachloride and triphenylphosphine)  
RN 156295-27-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,

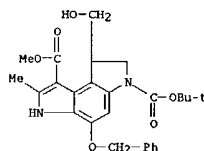
L14 ANSWER 77 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN  
AN 1994:483318 CAPLUS  
UN 121:83318  
TI Preparation of tetrahydropyrroloindole derivative and intermediates therefor  
IN Terashima, Shiro; Fukuda, Yasumichi  
PA Kyorin Pharmaceutical Co., Ltd., Japan; Sagami Chemical Research Center  
SO PCT Int. Appl., 24 pp.  
CODEN: PIXX02  
DT Patent  
LA Japanese  
FAN.CNT 1  
PATENT NO. KIND DATE APPLICATION NO. DATE  
PI WO 9404534 A1 19940303 WO 1993-JP1158 19930819  
W: AU, BB, BG, BR, CA, CZ, FI, HU, KR, LK, MG, MN, MW, NO, NZ, PL,  
RW: RO, RU, SD, SK, UA, US  
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,  
BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TC  
JP 06116270 A2 19940426 JP 1993-204254 19930818  
AU 9349811 A1 19940315 AU 1993-49811 19930819  
FRAI JP 1992-222861 A 19920821  
JP 1993-204254 A 19930818  
WO 1993-JP1158 W 19930819  
OS CASREACT 121:83318; MARPAT 121:83318  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Tetrahydropyrroloindole derivs. (I; R<sub>1</sub> = H or a hydroxyl-protecting group)  
R<sub>2</sub> = H or an amino-protecting group; X = halo, OH, alkylcarbonyloxy, arylcarbonyloxy, alkylsulfonyloxy, arylsulfonyloxy and optically active isomers thereof, useful as intermediates for a prospective anticancer agent KW-2189 (II.HCl), are prepared by reaction of aminoindoline derivs.  
(III; R = H; R<sub>3</sub> = HO-protective group; R<sub>4</sub> = H<sub>2</sub>N-protective group; X<sub>1</sub> = protected HO) with MeC.tplbond.CCO<sub>2</sub>Me, MeCOCH<sub>2</sub>CO<sub>2</sub>Me, or substituted Me crotonate and cyclization of the resulting Me (indolinylamino)crotonate  
III (R = OMe;CHCO<sub>2</sub>Me; R<sub>3</sub>, R<sub>4</sub>, X<sub>1</sub> = same as above) in the presence of a metal catalyst. Thus, (3S)-III (R = H, R<sub>3</sub> = PhCH<sub>2</sub>, R<sub>4</sub> = Me<sub>3</sub>CO<sub>2</sub>C, X<sub>1</sub> = OAc), MeCOCH<sub>2</sub>CO<sub>2</sub>Me, and p-MeC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>H.H<sub>2</sub>O were refluxed in benzene at 80° for 4 h to give (3S)-III (R = OMe;CHCO<sub>2</sub>Me; R<sub>3</sub>, R<sub>4</sub>, X<sub>1</sub> = same as above) which was heated in the presence of Pd(OAc)<sub>2</sub> in DMF at 70° for 4 h to give (3S)-I (R<sub>3</sub> = PhCH<sub>2</sub>, R<sub>4</sub> = Me<sub>3</sub>CO<sub>2</sub>C, X<sub>1</sub> = OAc). The latter

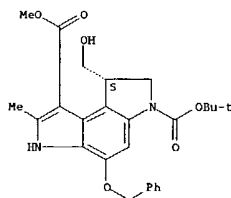
L14 ANSWER 77 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)

7,8-dihydro-8-(hydroxymethyl)-2-methyl-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



RN 156295-32-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-2-methyl-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

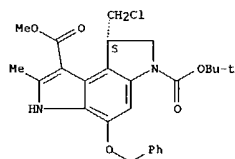


IT 156295-33-9P  
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);  
USES (Uses)  
(preparation and conversion of, into anticancer KW-2189)  
RN 156295-33-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-2-methyl-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

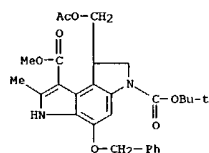
Absolute stereochemistry.

10/069,202

L14 ANSWER 77 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



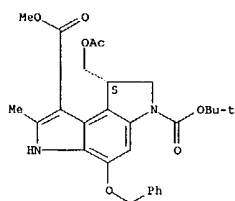
IT 156295-26-0P 156295-31-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (preparation and deacetylation of)  
 RN 156295-26-0 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
 8-[(acetyloxy)methyl]-7,8-dihydro-2-methyl-4-(phenylmethoxy)-,  
 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



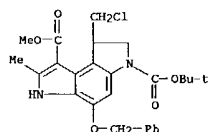
RN 156295-31-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
 8-[(acetyloxy)methyl]-7,8-dihydro-2-methyl-4-(phenylmethoxy)-,  
 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 77 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

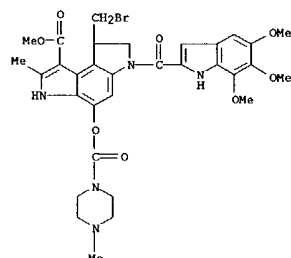


IT 156295-29-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (preparation and hydrogenolysis of)  
 RN 156295-29-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,  
 8-(chloromethyl)-7,8-dihydro-2-methyl-4-(phenylmethoxy)-,  
 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)

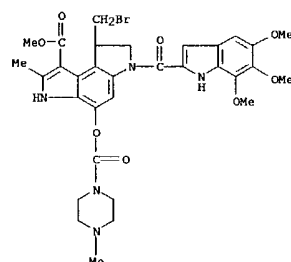


IT 134106-78-8P 134106-80-2P 154889-68-6P  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of, as anticancer agent)  
 RN 134106-78-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

L14 ANSWER 77 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 134106-80-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

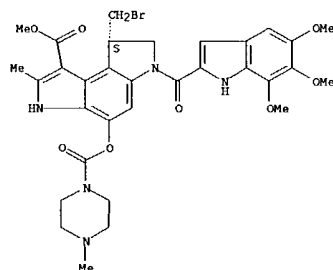


• HCl

L14 ANSWER 77 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

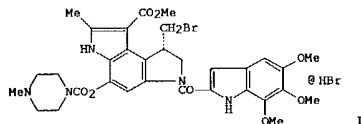
RN 154889-68-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



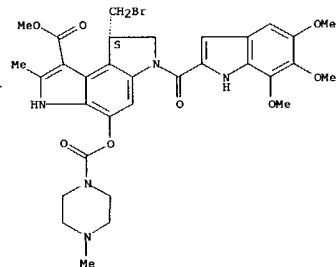
10/069,202

L14 ANSWER 78 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1994:315371 CAPLUS  
DN 120:315371  
TI Characteristics of antitumor activity of KW-2189, a novel  
water-soluble  
derivative of duocarmycin, against murine and human tumors  
AU Kobayashi, Eiji; Okamoto, Akihiko; Asada, Masao; Okabe, Masami;  
Nagamura, Satoru; Asai, Akira; Saito, Hiromitsu; Gomi, Katsushige; Hirata,  
Tadashi  
CS Pharm. Res. Lab., Kyowa Hekko Kogyo Co., Ltd., Nagazumi, 411, Japan  
SO Cancer Research (1994), 54(9), 2404-10  
CODEN: CNREAS; ISSN: 0008-5472  
DT Journal  
LA English  
GI



AB KW-2189 (I), a novel derivative of duocarmycin B2, was selected for  
extensive  
evaluation based on its improved antitumor activity, water  
solubility, and  
stability in the culture medium, as compared with duocarmycin B2.  
Although the in vitro cell growth-inhibitory activity of KW-2189 was  
less  
potent than that of duocarmycin B2, it significantly inhibited the  
growth  
of five murine solid tumors including Colon 26 adenocarcinoma, Colon  
38  
adenocarcinoma, and B16 melanoma in vivo. KW-2189 was also effective  
against murine P388 leukemia and L1210 leukemia not only by local  
administration (i.p.-i.p. system), but also by systemic  
administration  
(i.p.-i.v. or i.v.-i.v. system). The most remarkable feature of  
KW-2189  
was its efficacy against various human xenografts, which was  
observed in 14  
tumors among 16 tested tumors including drug-insensitive tumors by  
single  
i.v. administration. Tumor regression was observed in mice bearing  
LC-6

L14 ANSWER 78 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

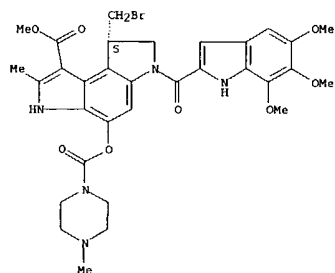


L14 ANSWER 78 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
lung, St-4 and St-40 stomach, Li-7 liver, PAN-2 pancreas, and MX-1  
breast  
carcinomas. In many cases, the activities of KW-2189 were more than  
those  
of clin. active agents, mitomycin C, Adriamycin, cisplatin, and  
cyclophosphamide. Delayed lethal toxicity, which was reported in mice  
treated with CC-1065 whose structure was similar to KW-2189, was not  
obsd.  
in mice treated with KW-2189. KW-2189 inhibited DNA synthesis more  
significantly than RNA or protein synthesis, although DNA strand  
breaks  
were not obsd. KW-2189 was activated by porcine liver esterase, mouse  
liver homogenate or Hep G2 homogenate, and DU-86-DNA adducts were  
detected  
in KW-2189-treated HeLa S3 cells, suggesting that KW-2189 was  
converted to  
DU-86 in the cells. These results indicate that KW-2189 is an  
interesting  
candidate for further development as a novel antitumor agent.  
IT 154889-68-6, KW 2189  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological  
study, unclassified); THU (Therapeutic use); BIOL (Biological study);  
USES  
(Uses)  
(antitumor activity of, in human and laboratory animal)  
RN 154889-68-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)-(9CI) (CA  
INDEX  
NAME)  
Absolute stereochemistry.

L14 ANSWER 79 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1994:315183 CAPLUS  
DN 120:315183  
TI A Novel Property of Duocarmycin and Its Analogs for Covalent Reaction  
with  
DNA  
AU Asai, Akira; Nagamura, Satoru; Saito, Hiromitsu  
CS Tokyo Research Laboratories, Kyowa Hekko Kogyo Co. Ltd., Machida,  
194,  
Japan  
SO Journal of the American Chemical Society (1994), 116(10), 4171-7  
CODEN: JACSAT; ISSN: 0002-7863  
DT Journal  
LA English  
AB For understanding the mechanism of action of antitumor agents and  
designing new drugs, the DNA alkylating property of duocarmycin (DUM)  
and  
its analogs was examined. The thermal depurination products of calf  
thymus  
DNA covalently bonded to DUMA were revealed to be not only the DUMA-N3  
adenine adduct but also unexpectedly the DUMA-N3 guanine adduct. In  
addition  
DUMSA and 2 synthetic analogs with higher solvolytic stability,  
reacted  
more selectively with N3 adenine than DUMA did. The correlation  
between  
electrophilicity of the cyclopropanesubunit in the mol. and  
selectivity to  
adenine was observed. KW-2189, a synthetic derivative which has  
improved in vivo  
antitumor activity, was designed as a prodrug requiring enzymic  
hydrolysis  
of the carbamoyl moiety, followed by the drug regeneration.  
Surprisingly  
the authors discovered that KW-2189 itself alkylated DNA covalently  
without release of the carbamoyl moiety. For the mechanism of DNA  
alkylation by KW-2189, a novel alkylating reaction via the formation  
of an  
iminium intermediate without loss of the carbamoyl moiety was  
proposed.  
IT 154889-68-6, KW 2189  
RL: PRP (Properties)  
(DNA alkylating property of, structure effect on)  
RN 154889-68-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)-(9CI) (CA  
INDEX  
NAME)  
Absolute stereochemistry.

10/069,202

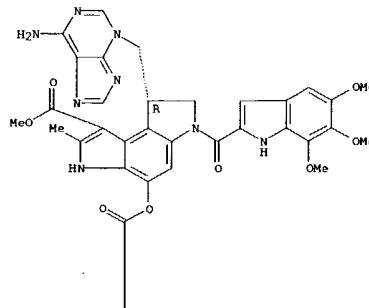
L14 ANSWER 79 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



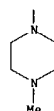
IT 154715-67-0 154715-68-1 154901-65-2  
 RL: FORM (Formation, nonpreparative)  
 (formation of, antitumor activity in relation to)  
 RN 154715-67-0 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 6-[(6-amino-3H-purin-3-yl)methyl]-3,6,7,8-tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyloxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (R)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry.

L14 ANSWER 79 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

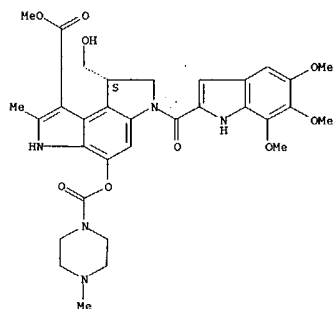


PAGE 2-A

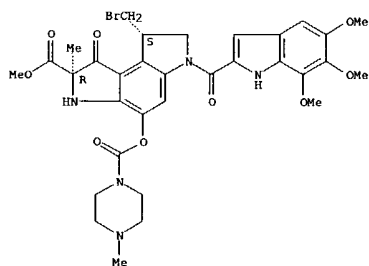


RN 154715-68-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyloxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry.

L14 ANSWER 79 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 154901-65-2 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyloxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry.



L14 ANSWER 79 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

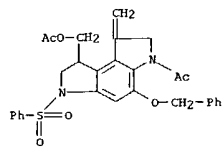
10/069,202

L14 ANSWER 80 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1994:217053 CAPLUS  
 DN 120:217053  
 TI Synthesis of (±)-N2-(benzenesulfonyl)-CPI, the protected A-unit of  
 the  
 antitumor antibiotic CC-1065, by two metal-initiated cyclizations  
 AU Tietze, Lutz F.; Grote, Thomas  
 CS Inst. Org. Chem., Georg-August-Univ., Goettingen, D-37077, Germany  
 SO Journal of Organic Chemistry (1994), 59(1), 192-6  
 CODEN: JOCEAH; ISSN: 0022-3263  
 DT Journal  
 LA English  
 OS CASREACT 120:217053  
 GI

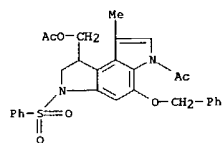
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB A new synthetic route to (±)-N2-(Benzenesulfonyl)-CPI (I), the  
 protected A-unit containing a cyclopropylhexadienone moiety of the  
 highly  
 potent antitumor antibiotic CC-1065, from  
 5-(benzyloxy)-2-bromophenylamine  
 is described. The key steps are a zirconium- and a  
 palladium-initiated  
 cyclization to give the two pyrrole moieties. Reaction of  
 N-allyl-N-(benzenesulfonyl)bromophenylamine II with  
 zirconocene(methyl)  
 chloride leads after workup with I2 to the 4-iodoindoline III, which  
 was  
 transformed into (allylamino)iodoindole IV and subsequently via Heck  
 reaction into the pyrroloindoline V.  
 IT 153914-88-6 153914-89-7  
 RL: RCT (Reactant); RAC (Reactant or reagent)  
 (preparation as intermediate, synthesis of (benzenesulfonyl)-CPI)  
 RN 153914-88-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol,  
 6-acetyl-1,2,3,6,7,8-hexahydro-8-  
 methylene-5-(phenylmethoxy)-3-(phenylsulfonyl)-, acetate (ester)  
 (9CI)  
 (CA INDEX NAME)

L14 ANSWER 80 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

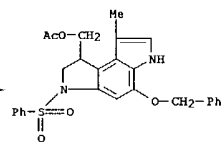


RN 153914-89-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol,  
 6-acetyl-1,2,3,6-tetrahydro-8-  
 methyl-5-(phenylmethoxy)-3-(phenylsulfonyl)-, acetate (ester) (9CI)  
 (CA INDEX NAME)



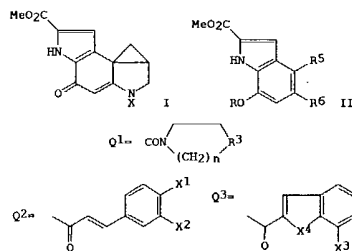
IT 153914-90-0P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, as intermediate, synthesis of  
 (benzenesulfonyl)-CPI)  
 RN 153914-90-0 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol,  
 1,2,3,6-tetrahydro-8-methyl-5-  
 (phenylmethoxy)-3-(phenylsulfonyl)-, acetate (ester) (9CI) (CA INDEX  
 NAME)

L14 ANSWER 80 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 81 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1994:163825 CAPLUS  
 DN 120:163825  
 TI Preparation of DC 113 derivatives as antitumor or antimicrobial agents  
 IN Nagamura, Akihito; Saito, Hiromitsu; Ogawa, Tatsuhiro; Katsumata,  
 Shigeo;  
 Mihara, Akira; Takahashi, Keiichi; Kobayashi, Eiji; Gomi, Katsunari  
 PA Kyowa Hakko Kogyo Kk, Japan  
 SO Jpn. Kokai Tokkyo Koho, 15 pp.  
 CODEN: JKKXAF  
 DT Patent  
 LA Japanese  
 FAN.CNT 1  

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05208979	A2	19930820	JP 1992-153534	19920612
PRAI JP 1991-158897		19910628		
OS MARPAT 120:163825				
GI				



AB The title compds. I, II [R = H, CONR1R2, Q1; R1, R2 = H, lower alkyl;  
 R3 =  
 CH2, O, NMe; R5R6 = CH(CH2Z)CH2NX, CH2CH(CH2Z)CH2NX; X = H, Q2, Q3;  
 X1-3 =  
 H, OR4; X4 = NH, O; R4 = lower alkyl; Z = Cl, Br; n = 0-4; if X in I  
 = Q3  
 and X4 = NH, then X1, X2, and/or X3 = H], or their salts are prepared  
 DC  
 113 in MeCN was treated with HCl at room temperature for 1 h and the  
 reaction  
 product was treated with p-nitrophenyl chloroformate and NET3 in  
 CH2Cl2 at  
 -50° for 0.5 h followed by Me2NH at -50° to room temperature for  
 0.5 h to give 57% II (R = CONMe2, R5R6 = CH(CH2Cl)CH2NX, X = Q3, X1-3  
 =

10/069,202

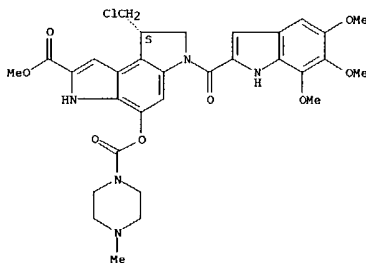
L14 ANSWER 81 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
OMe, X4 = NH), which inhibited growth of HeLa53 cells with IC50 of 0.78

nM.  
IT 152718-02-0P 152718-03-1P 152718-04-2P  
152718-05-3P 152718-07-5P 152718-08-6P  
152718-09-7P 152718-10-0P 152718-11-1P  
R1: SPN (Synthetic preparation): PREP (Preparation)  
(preparation of, as antitumor and antimicrobial agent)

RN 152718-02-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-

tetrahydro-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

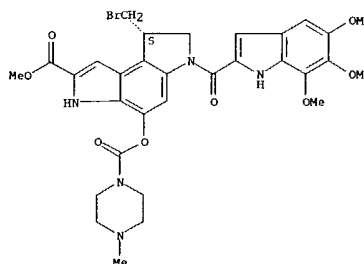


RN 152718-03-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

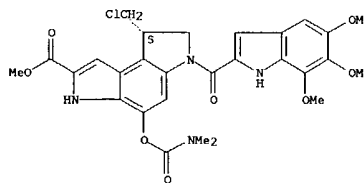
Absolute stereochemistry.

L14 ANSWER 81 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 152718-04-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-4-[[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

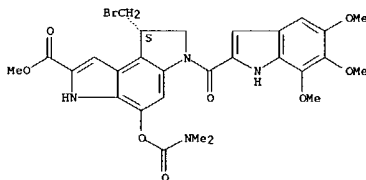
Absolute stereochemistry.



RN 152718-05-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

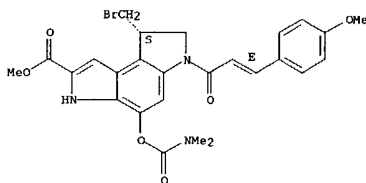
Absolute stereochemistry.

L14 ANSWER 81 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 152718-07-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(3-(4-methoxyphenyl)-1-oxo-2-propenyl)-, methyl ester, (S)-(E)- (9CI) (CA INDEX NAME)

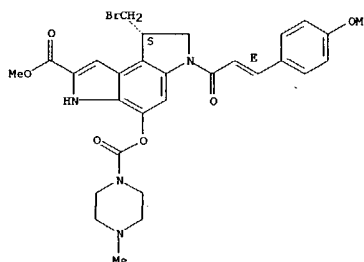
Absolute stereochemistry.  
Double bond geometry as shown.



RN 152718-08-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-tetrahydro-6-[[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (S)-(E)- (9CI) (CA INDEX NAME)

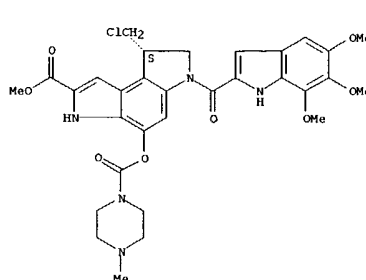
Absolute stereochemistry.  
Double bond geometry as shown.

L14 ANSWER 81 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 152718-09-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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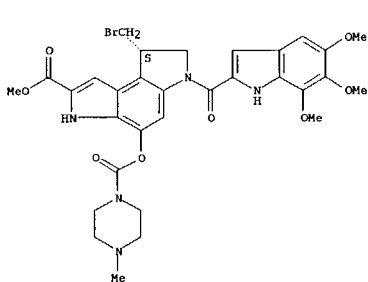
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L14 ANSWER 81 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
PAGE 2-A

● HCl

RN 152718-10-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-  
1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (S)-  
(9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



PAGE 1-A

PAGE 2-A

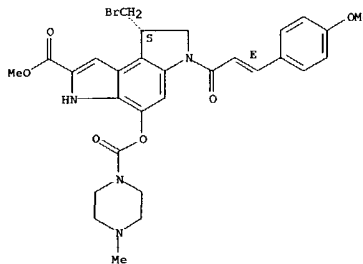
● HCl

RN 152718-11-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-  
tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-4-[[[(4-methyl-1-  
piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride, [S-(E)]-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 81 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
Double bond geometry as shown.

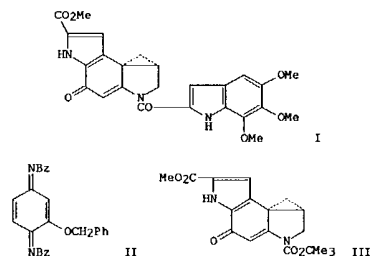
PAGE 1-A



PAGE 2-A

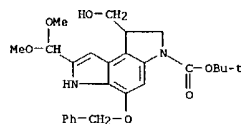
● HCl

L14 ANSWER 82 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1993:649750 CAPLUS  
DN 119:249750  
TI Total synthesis and preliminary evaluation of (+)- and  
ent-(-)-duocarmycin  
SA  
AU Boger, Dale L.; Machiya, Kozo; Hertzog, Donald L.; Kito, Paul A.;  
Holmes,  
Daniel  
CS Dep. Chem., Scripps Res. Inst., La Jolla, CA, 92037, USA  
SO Journal of the American Chemical Society (1993), 115(20), 9025-36  
CODEN: JACSAT; ISSN: 0002-7863  
DT Journal  
LA English  
GI



AB Concise total syntheses of natural (+)- (I) and ent-(-)-duocarmycin  
SA are  
based on sequential regioselective nucleophilic substitution  
reactions of  
the unsym. p-quinonediimine II in the preparation of a  
dihydropyrroloindole  
precursor to the left-hand subunit. In addition to constituting a  
new  
synthetic strategy for the preparation of I and related agents, both  
enantiomers of N-BOC-USA (III) and its immediate synthetic  
precursors are  
made available by the approach. This provides access to synthetic  
analogues  
incorporating either enantiomer of the exceptionally stable and  
potent  
duocarmycin SA alkylation subunit. Studies reveal that III is 4.8  
times

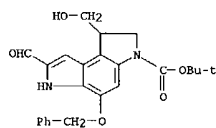
L14 ANSWER 82 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
more stable to chem. solvolysis than N-BOC-CPI, the authentic  
alkylation  
subunit of CC-1065, and that the agents participate in a  
stereoelectronically-controlled solvolysis reaction with nucleophilic  
addn. to the least hindered cyclopropane carbon. Consistent with this  
enhanced stability, (+)-III had the most potent inherent cytotoxic  
activity of all natural and synthetic alkylation subunits examd. to  
date  
including (+)-N-BOC-CPI, and its relative cytotoxic potency  
predictably  
follows a fundamental relationship between chem. stability and  
cytotoxic  
potency established in prior studies. In contrast to expectations  
based  
on past observations, the unnatural enantiomers of I and III also  
constituted potent cytotoxic agents whose further examn. should prove  
exceptionally interesting.  
IT 144667-33-4P 144667-34-5P 144667-35-6P  
144667-39-0P 144732-56-9P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(intermediate in preparation of duocarmycin SA)  
RN 144667-33-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
7-(dimethoxymethyl)-  
1,6-dihydro-1-(hydroxymethyl)-5-(phenylmethoxy)-, 1,1-dimethylethyl  
ester  
(9CI) (CA INDEX NAME)



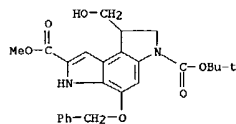
RN 144667-34-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
7-formyl-1,6-dihydro-1-  
(hydroxymethyl)-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA  
INDEX NAME)

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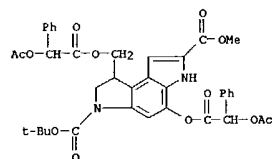
L14 ANSWER 82 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



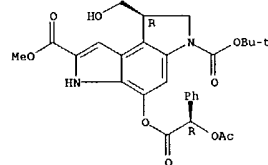
RN 144667-35-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,  
7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-,  
6-(1,1-dimethylethyl)  
2-methyl ester (9CI) (CA INDEX NAME)



RN 144667-39-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,  
4-[[[(acetyloxy)phenylacetyl]oxy]-8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-  
7,8-dihydro-, 6-(1,1-dimethylethyl) 2-methyl ester,  
[8R-[4(R\*),8R\*(R\*)]]-  
(9CI) (CA INDEX NAME)

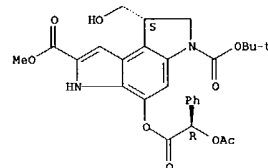


L14 ANSWER 82 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 150992-79-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,  
4-[[[(acetyloxy)phenylacetyl]oxy]-8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-  
7,8-dihydro-8-(hydroxymethyl)-,  
6-(1,1-dimethylethyl) 2-methyl ester, [R-(R\*,S\*)]]- (9CI) (CA INDEX  
NAME)

Absolute stereochemistry.

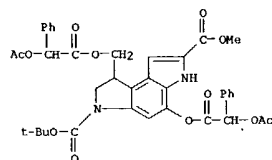


RN 150992-80-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,  
8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-7,8-dihydro-4-(phenylmethoxy)-,  
6-(1,1-dimethylethyl) 2-methyl ester, [R-(R\*,R\*)]]- (9CI) (CA INDEX  
NAME)

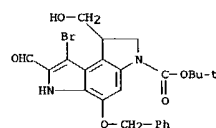
Absolute stereochemistry.

L14 ANSWER 82 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 144732-56-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,  
4-[[[(acetyloxy)phenylacetyl]oxy]-8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-  
7,8-dihydro-, 6-(1,1-dimethylethyl) 2-methyl ester,  
[8S-[4(S\*),8R\*(S\*)]]-  
(9CI) (CA INDEX NAME)



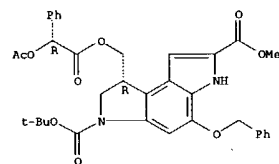
IT 150992-77-1P 150992-78-2P 150992-79-3P  
150992-80-6P 150992-81-7P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)  
RN 150992-77-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
8-bromo-7-formyl-1,6-  
dihydro-1-(hydroxymethyl)-5-(phenylmethoxy)-, 1,1-dimethylethyl ester  
(9CI) (CA INDEX NAME)



RN 150992-78-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,  
4-[[[(acetyloxy)phenylacetyl]oxy]-8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-  
7,8-dihydro-8-(hydroxymethyl)-,  
6-(1,1-dimethylethyl) 2-methyl ester, [R-(R\*,R\*)]]- (9CI) (CA INDEX  
NAME)

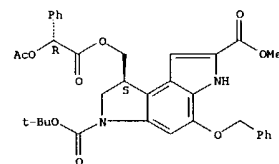
Absolute stereochemistry.

L14 ANSWER 82 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



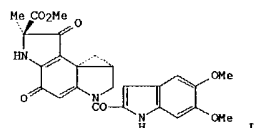
RN 150992-81-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,  
8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-7,8-dihydro-4-(phenylmethoxy)-,  
6-(1,1-dimethylethyl) 2-methyl ester, [R-(R\*,S\*)]]- (9CI) (CA INDEX  
NAME)

Absolute stereochemistry.



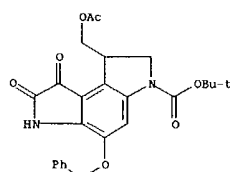
10/069,202

L14 ANSWER 83 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1993:538951 CAPLUS  
 DN 119:138951  
 TI Synthesis and cytotoxicity of enantiomeric pairs of duocarmycin A and its 2-epimer  
 AU Fukuda, Yasumichi; Nakatani, Kazuhiko; Terashima, Shiro  
 CS Cent. Res. Lab., Kyorin Pharm. Co., Ltd., Nogai, 329-01, Japan  
 SO Bioorganic & Medicinal Chemistry Letters (1992), 2 (7), 755-8  
 CODEN: BMCLE8; ISSN: 0960-894X  
 DT Journal  
 LA English  
 GI

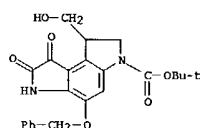


AB The synthesis of the four possible diastereomers of duocarmycin A (I) was achieved through optical resolution of a tricyclic synthetic intermediate.  
 The stereochem. configuration of the cyclopropane ring was found to be closely related with their cytotoxicity against P388 murine leukemia.  
 IT 132628-62-7  
 RL: RCT (Reactant); RACT (Reactant or reagent) (deacetylation of)  
 RN 132628-62-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[(acetyloxy)methyl]-  
 1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester  
 (9CI) (CA INDEX NAME)

L14 ANSWER 83 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



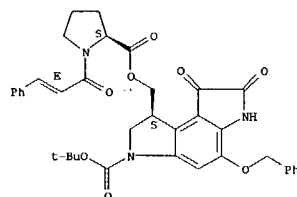
IT 143874-46-8P  
 RL: SPN (Synthetic preparation); PREP (Preparation) (preparation and acylation with cinnamoylproline, and resolution of)  
 RN 143874-46-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6,7,8-tetrahydro-1-(hydroxymethyl)-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester  
 (9CI) (CA INDEX NAME)



IT 149365-69-5P 149365-70-8P 149405-53-8P  
 149405-54-9P 149405-56-1P 149405-57-2P  
 RL: SPN (Synthetic preparation); PREP (Preparation) (preparation and conversion of, to duocarmycin)  
 RN 149365-69-5 CAPLUS  
 CN L-Proline, 1-[(1-oxo-3-phenyl-2-propenyl)-, [3-[(1,1-dimethylethoxy)carbonyl]-1,2,3,6,7,8-hexahydro-7,8-dioxo-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl)methyl ester, (S)-  
 (9CI) (CA INDEX NAME)

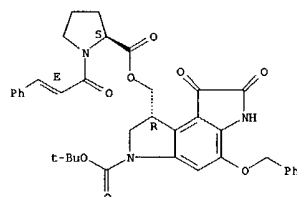
Absolute stereochemistry.  
 Double bond geometry as shown.

L14 ANSWER 83 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 149365-70-8 CAPLUS  
 CN L-Proline, 1-[(1-oxo-3-phenyl-2-propenyl)-, [3-[(1,1-dimethylethoxy)carbonyl]-1,2,3,6,7,8-hexahydro-7,8-dioxo-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl)methyl ester, (R)-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.

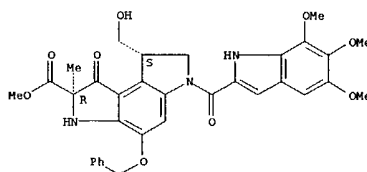


RN 149405-53-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-

(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

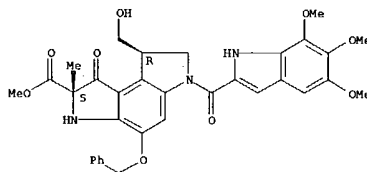
Absolute stereochemistry. Rotation (+).

L14 ANSWER 83 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 149405-54-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

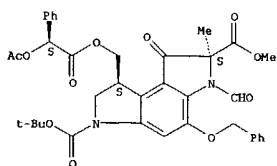


RN 149405-56-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 6-(1,1-dimethylethyl) ester, [2S-[2α,8α(R\*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

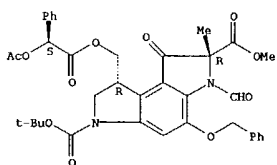
10/069,202

L14 ANSWER 83 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)



RN 149405-57-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,  
8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 6-(1,1-dimethylethyl) ester, [2R-[2 $\alpha$ ,8 $\alpha$ (S\*)]]- (9CI) (CA INDEX NAME)

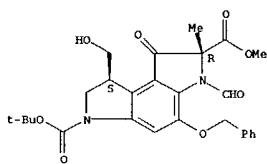
Absolute stereochemistry. Rotation (+).



IT 132628-67-2P 132628-68-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT (Reactant or reagent)  
(preparation and desilylation of)  
RN 132628-67-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,  
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, trans- (9CI) (CA INDEX NAME)

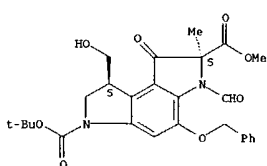
Relative stereochemistry.

L14 ANSWER 83 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)



RN 149365-67-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3,7(2H)-dicarboxylic acid,  
6-formyl-1,6,7,8-tetrahydro-1-(hydroxymethyl)-7-methyl-8-oxo-5-(phenylmethoxy)-, 3-(1,1-dimethylethyl) 7-methyl ester, cis- (9CI) (CA INDEX NAME)

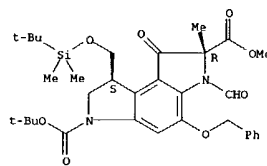
Relative stereochemistry.



IT 149365-68-4P 149405-52-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT (Reactant or reagent)  
(preparation, hydrolysis, and acylation of, with indolylcarboxylate)  
RN 149365-68-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,  
8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, [2R-[2 $\alpha$ ,8 $\beta$ (S\*)]]- (9CI) (CA INDEX NAME)

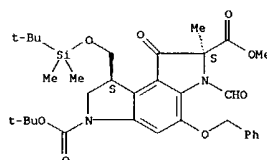
Absolute stereochemistry. Rotation (+).

L14 ANSWER 83 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)



RN 132628-68-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,  
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, cis- (9CI) (CA INDEX NAME)

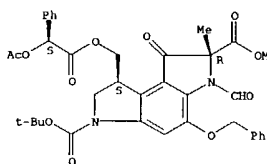
Relative stereochemistry.



IT 149365-66-2P 149365-67-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT (Reactant or reagent)  
(preparation, acylation, and resolution of)  
RN 149365-66-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,  
3-formyl-2,3,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, trans- (9CI) (CA INDEX NAME)

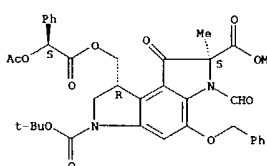
Relative stereochemistry.

L14 ANSWER 83 OF 112 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)



RN 149405-52-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,  
8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 6-(1,1-dimethylethyl) ester, [2S-[2 $\alpha$ ,8 $\beta$ (R\*)]]- (9CI) (CA INDEX NAME)

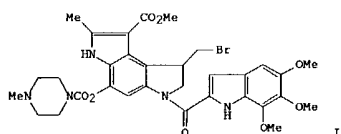
Absolute stereochemistry. Rotation (-).



10/069,202

L14 ANSWER 84 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1993:456138 CAPLUS  
 DN 119:56138  
 TI Hydrobromide of antitumor DC-89 with high stability  
 IN Nagamura, Satoru; Saito, Hiromitsu; Hayakawa, Eiji; Kato, Yasuki;  
 Naganuma, Hirotake  
 PA Kyowa Hakko Kogyo Co., Ltd., Japan  
 SO Eur. Pat. Appl., 6 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CWT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 537575	A1	19930421	EP 1992-116898	19921002
	R: DE, FR, GB, IT				
	JP 05097853	A2	19930420	JP 1991-259188	19911007
	CA 2079733	AA	19930408	CA 1992-2079733	19921002
PRAI	JP 1991-259188		19911007		
GI					



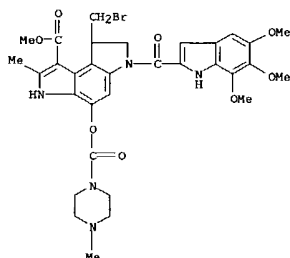
AB Hydrobromide of antitumor DC-89 (I) with high stability in solns. for producing freeze-dried preps. are prepared by reaction of HBr with the base. The residual rate of a solution of 1 mg I/mL at 25° after 6 h was 98 %. Antitumor activity of I against sarcoma tumor was equal to its HCl salt.

IT 148778-32-9P  
 RL: PREP (Preparation)  
 (preparation of, with high stability in solns.)

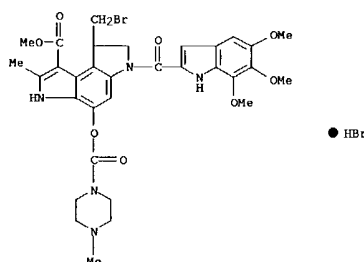
RN 148778-32-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide (9CI)  
 (CA INDEX NAME)

L14 ANSWER 84 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 84 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 134106-78-8  
 RL: PROC (Process)  
 (salt formation of, with hydrobromic acid, with high stability in solns.)

RN 134106-78-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 85 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1993:191718 CAPLUS  
 DN 118:191718  
 TI Preparation of DC-89 derivatives as neoplasm inhibitors and antibacterials  
 IN Nagamura, Satoru; Saito, Hiromitsu; Kobayashi, Eiji; Gomi, Katsushige  
 PA Kyowa Hakko Kogyo Co., Ltd., Japan  
 SO Eur. Pat. Appl., 20 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CWT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 520435	A2	19921230	EP 1992-110688	19920625
	EP 520435	A3	19930505		
	R: DE, FR, GB, IT				
	JP 05178858	A2	19930720	JP 1992-167102	19920625
	US 5258393	A	19931102	US 1992-903756	19920625
PRAI	JP 1991-158896		19910628		
OS	MARPAT 118:191718				
GI					

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

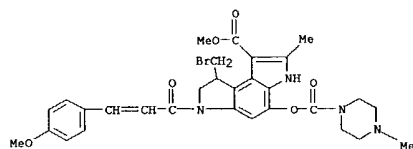
AB Title compds. (I: X = H, CO2Me; Q = Q1, Q2; W = H, Q3; W1, W2 = H, OR4; R4 = alkyl, alkenyl; Z = Cl, Br; R = H, carbamoyl), were prepared Thus, precursor II was N-deacetylated with NaOMe in MeOH (99% yield) and the product was condensed with 4-nitrophenyl 4-methoxycinnamate using NaH in DMF (85% yield). The cinnamide was stirred with 48% HBr in MeCN to give a residue which in CH2Cl2 was treated sequentially p-nitrophenyl chloroformate, Et3N, and aq- Me2NH to give 90% title compound III. III at 8.0 mg/kg i.v. in mice implanted with sarcoma 180 tumors reduced tumor volume to 2-7% of the volume of untreated controls.

IT 146910-07-8P 146910-08-9P 146910-09-0P  
 146940-70-7P 146940-71-8P 146940-72-2P  
 146940-73-0P 146940-74-1P 146940-75-2P  
 146940-76-3P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of, as neoplasm inhibitor)

RN 146910-07-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride (9CI)  
 (CA

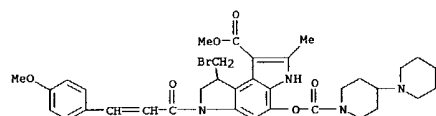
10/069,202

L14 ANSWER 85 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
INDEX NAME)

● HCl

RN 146910-08-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
4-[[[(1,4'-bipiperidin)-1'-ylcarbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, monohydrochloride (9CI)

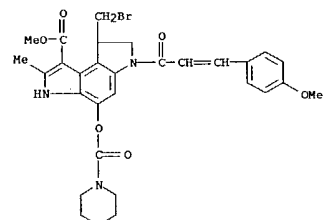
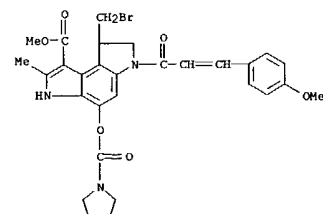
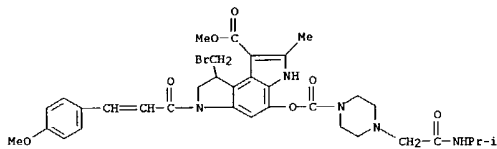
(CA INDEX NAME)



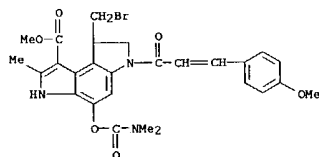
● HCl

RN 146910-09-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methylethylamino)-2-oxoethyl]-1-piperazinyl]carbonyl]oxy-, methyl ester,

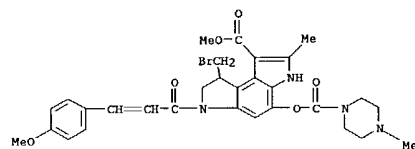
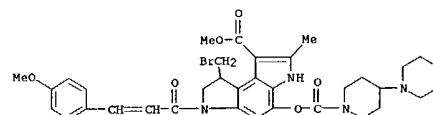
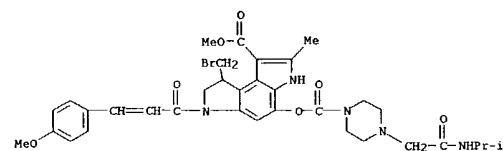
L14 ANSWER 85 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 146940-72-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(1-pyrrolidinylcarbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)RN 146940-73-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)L14 ANSWER 85 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 146940-70-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)RN 146940-71-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(1-piperidinylcarbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

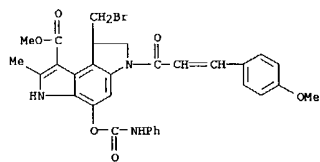
L14 ANSWER 85 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 146940-74-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
4-[[[(1,4'-bipiperidin)-1'-ylcarbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)RN 146940-75-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

RN 146940-76-3 CAPLUS

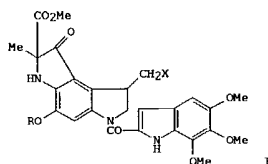
10/069,202

L14 ANSWER 86 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
 8-(bromomethyl)-3,6,7,8-  
 tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-  
 [(phenylamino)carbonyloxy]-, methyl ester (9CI) (CA INDEX NAME)



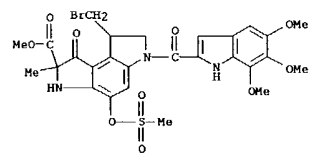
L14 ANSWER 86 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1993:38908 CAPLUS  
 DN 118:38908  
 TI Preparation of DC-89 derivatives  
 IN Saito, Hiromitsu; Nagamura, Satoru; Kobayashi, Eiji; Gomi, Katsushige  
 PA Kyowa Hakko Kogyo Co., Ltd., Japan  
 SO Eur. Pat. Appl., 19 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CNT 1  

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 499130	A1	19920819	EP 1992-101913	19920205
R: DE, FR, GB, IT				
JP 05051384	A2	19930302	JP 1992-20059	19920205
PRAI JP 1991-21243		19910215		
OS MARPAT 118:38908				
GI				

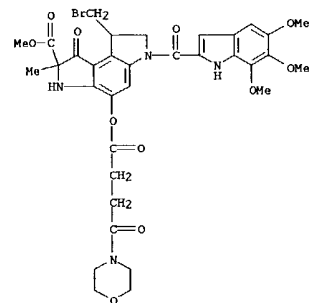


AB Title compds. I (X = Br, Cl; R = R1O2S, CO(CH2)nR2, wherein R1 = C1-6 alkyl, Ph, R2 = substituted heterocyclyl, n = 0-5) or a salt thereof, useful as antitumor agents, are prepared To DC-89B2 in CH2Cl2 was added DCC in CH2Cl2 followed by 3-(4-morpholinocarbonyl)propionic acid in CH2Cl2 to give I (X = Br, R = 4-morpholino-1-oxobutanoyl) (II). The IC50 of II on growth inhibitory effect against HeLa53 cells was 0.054 nM.  
 IT 144258-83-3P 144258-84-4P 144258-85-5P  
 144258-86-6P 144258-87-7P 144258-88-8P  
 144258-89-9P 144258-90-2P 144258-91-3P  
 144258-92-4P 144258-93-5P 144258-94-6P  
 144773-23-9P 144773-24-0P 144773-25-1P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

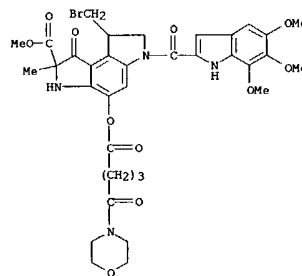
L14 ANSWER 86 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of, as antitumor agent)  
 RN 144258-83-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
 1,2,3,6,7,8-hexahydro-2-methyl-4-[(methylsulfonyl)oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



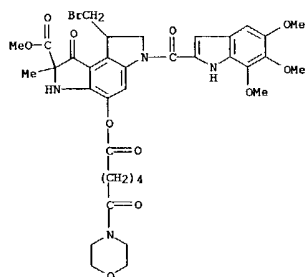
RN 144258-84-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
 1,2,3,6,7,8-hexahydro-2-methyl-4-[(4-(4-morpholinyl)-1,4-dioxobutoxy)-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 86 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 RN 144258-85-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
 1,2,3,6,7,8-hexahydro-2-methyl-4-[(5-(4-morpholinyl)-1,5-dioxopentyl)oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 144258-86-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
 1,2,3,6,7,8-hexahydro-2-methyl-4-[(6-(4-morpholinyl)-1,6-dioxohexyl)oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

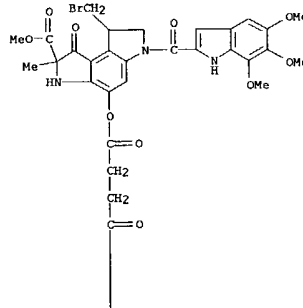


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RN 144258-87-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-4-[4-(4-methyl-1-piperazinyl)-1,4-
dioxobutoxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,
methyl
      ester (9CI) (CA INDEX NAME)

```

PAGE 1-A



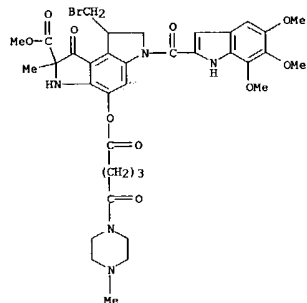
PAGE 2-A



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RN      144258-88-8  CAPLUS
CN      Benzo[1,2-b:4,3-b']dipyrrrole-2-carboxylic acid, 8-(bromomethyl)-
        1,2,3,6,7,8-hexahydro-2-methyl-4-[[5-(4-methyl-1-piperazinyl)-1,5-
        dioxopentyl]oxy]-1-oxo-6-[[5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,
        methyl ester (9CI)  (CA INDEX NAME)

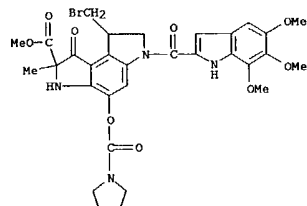
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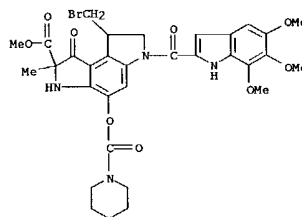
RN      144258-89-9  CAPLUS
CN      Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[(1-pyrrolidinylcarbonyl)oxy]-6-
[5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA
INDEX
NAME)

```



RN 144258-90-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[(1-piperidinylcarbonyl)oxy]-6-  
{(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl}-, methyl ester (9CI) (CA  
INDEX

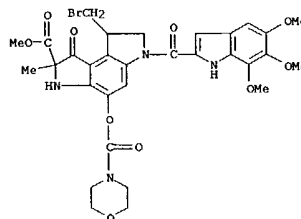
NAME)



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RN      144258-91-3  CAPLUS
CN      Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
        1,2,3,6,7,8-hexahydro-2-methyl-4-[(4-morpholinylcarbonyl)oxy]-1-oxo-6-
        [(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI)  (CA
INDEX
NAME)

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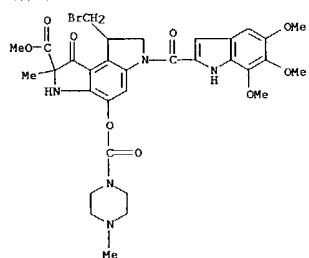
RN      144258-92-4  CAPIUS
CN      Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-4-[[4-(4-methyl-1-piperazinyl)carbonyl]oxy]-1-
oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI)
(CA
INDEX NAME)

```

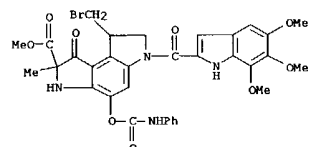


10/069,202

L14 ANSWER 86 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

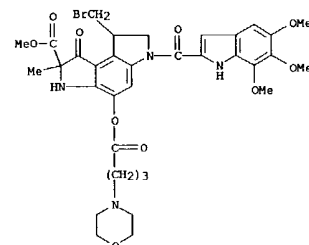


RN 144258-93-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
1,2,3,6,7,8-hexahydro-2-methyl-4-[[[(phenylamino)carbonyl]oxy]-6-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

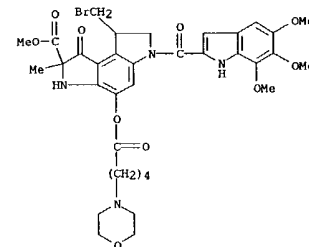


RN 144258-94-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-  
1,2,3,6,7,8-hexahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

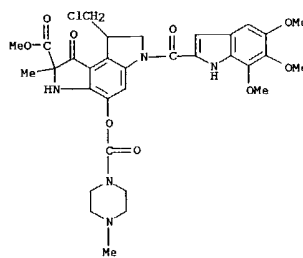
L14 ANSWER 86 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



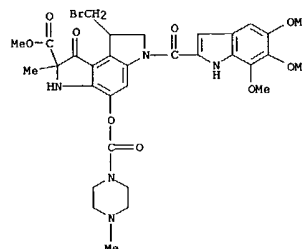
RN 144773-25-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
1,2,3,6,7,8-hexahydro-2-methyl-4-[[[(5-(4-morpholinyl)-1-oxopentyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



L14 ANSWER 86 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

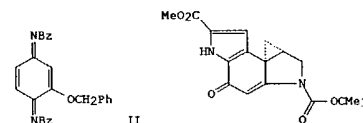
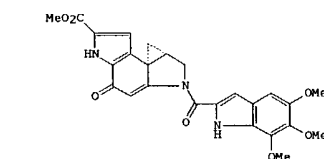


RN 144773-23-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
1,2,3,6,7,8-hexahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



RN 144773-24-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
1,2,3,6,7,8-hexahydro-2-methyl-4-[[[(4-morpholinyl)-1-oxobutoxy]-6-[(5,6,7-

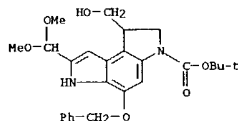
L14 ANSWER 87 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1993:38646 CAPLUS  
DN 118:38646  
TI Total synthesis of (+)-duocarmycin SA  
AU Boger, Dale L.; Machiya, Kozi  
CS Dep. Chem., Scripps Res. Inst., La Jolla, CA, 92037, USA  
SO Journal of the American Chemical Society (1992), 114(25), 10056-8  
CODEN: JACSAT; ISSN: 0002-7863  
Journal  
LA English  
OS CASREACT 118:38646  
GI



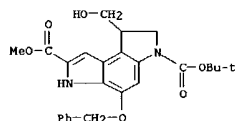
AB A concise total synthesis of natural (+)-duocarmycin SA (I) is based on sequential regioselective nucleophilic substitution reactions of the unsym. p-quinone diimide II leading to a dihydropyrroloindole precursor to the left-hand subunit. In addition to constituting a new synthetic strategy for the preparation of agents related to the natural or synthetic members of the duocarmycin class of antitumor-antibiotics, both enantiomers of N-BOC DSA (III) and its immediate synthetic precursors are now available. This provides access to synthetic analogs incorporating either enantiomer of the exceptionally stable and potent duocarmycin SA alkylation subunit.  
IT 144667-33-4p

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L14 ANSWER 87 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (prepn. and acetal hydrolysis of)  
 RN 144667-33-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
 7-(dimethoxymethyl)-  
 1,6-dihydro-1-(hydroxymethyl)-5-(phenylmethoxy)-, 1,1-dimethylethyl  
 ester (9CI) (CA INDEX NAME)

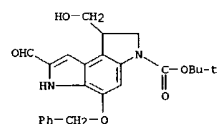


IT 144667-35-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (preparation and hydrogenolysis of)  
 RN 144667-35-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,  
 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-,  
 6-(1,1-dimethylethyl)  
 2-methyl ester (9CI) (CA INDEX NAME)

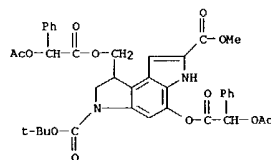


IT 144667-39-0P 144732-56-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (preparation and hydrolysis of)  
 RN 144667-39-0 CAPLUS

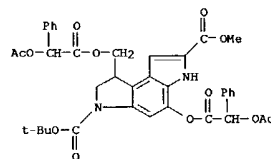
L14 ANSWER 87 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 INDEX NAME)



L14 ANSWER 87 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,  
 4-[[[(acetyloxy)phenylacetyl]oxy]-8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-  
 7,8-dihydro-, 6-(1,1-dimethylethyl) 2-methyl ester,  
 [8R-[4(R\*),8R\*(R\*)]]-  
 (9CI) (CA INDEX NAME)



RN 144732-56-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,  
 4-[[[(acetyloxy)phenylacetyl]oxy]-8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-  
 7,8-dihydro-, 6-(1,1-dimethylethyl) 2-methyl ester,  
 [8S-[4(S\*),8R\*(R\*)]]-  
 (9CI) (CA INDEX NAME)

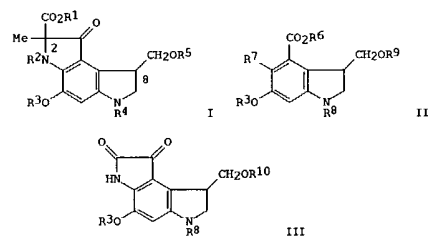


IT 144667-34-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (preparation and oxidation of)  
 RN 144667-34-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
 7-formyl-1,6-dihydro-1-  
 (hydroxymethyl)-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA

L14 ANSWER 88 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1992:591827 CAPLUS  
 DN 117:191827  
 TI Preparation of 2-alkoxycarbonyl-2-methyl-1-oxo-1,2,3,6,7,8-  
 hexahydrobenzo[1,2-b:4,3-b']dipyrrole derivatives as intermediates for  
 duocarmycin  
 IN Terajima, Atsuro; Fukuda, Yasumichi; Nakatani, Kazuhiko; Ito, Yoshio  
 PA Sagami Chemical Research Center, Japan  
 SO Jpn. Kokai Tokkyo Koho, 27 pp.  
 CODEN: JKKXAF  
 DT Patent  
 LA Japanese  
 FAN.CNT 1  

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04117383	A2	19920417	JP 1990-159828	19900620
JP 3037965	B2	20000508		
JP 1990-159828		19900620		
JP 1990-159828		19900620		

 PI  
 PRAI  
 OS  
 GI



AB The title compds. (I; R1 = H, C1-6 linear or branched alkyl; R2, R4 =  
 H,  
 amino-protecting group; R3, R5 = H, hydroxy-protecting group) and  
 their  
 intermediates [II and III; R3, R9, R10 = H, hydroxy-protecting group;  
 R6 =  
 H, C1-6 linear or branched alkyl; R7 = (un)substituted amino; R8 = H,  
 amino-protecting group] are prepared I are useful as intermediates  
 for the  
 anticancer agents duocarmycin A, B1, C1 (pyrindamycin B), and C2  
 (pyrindamycin A). Thus, oxidation of III (R3 = PhCH2, R8 = CO2OMe3,  
 R10 =  
 SiMe2OMe3) (preparation given) with m-ClC6H4CO2OH in CH2Cl2 and  
 methanolysis of  
 the resulting isatoic acid anhydride derivative in the presence of  
 K2CO3 gave

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L14 ANSWER 88 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
II (R3 = PhCH2, R6 = Me, R7 = H2N, R8 = CO2Me3, R9 = SiMe2CMe3).  
Alkylation of this with BrCHMeCO2Me in the presence of Cs2CO3 in DMF

and  
formylation of the resultant II (R7 = NHCHMeCO2Me; R3, R6-R9 = same  
as  
above) gave II [R7 = N(CHO)CHMeCO2Me; R3, R6-R9 = same as above],  
which

was cyclized by treatment with (Me2CH)2NLi in THF at -78° for 5.5 h  
to give (2R\*,8S\*)- and (2S\*,8S\*)-I (R1 = Me, R2 = CHO, R3 = PhCH2,  
R4 =

CO2CMe3, R5 = SiMe2CMe3). These were converted into dl-duocarmycin  
A or

-epiduocarmycin A.

IT 132628-61-6P 132628-62-7P 132628-63-8P

132628-67-2P 132628-68-3P 132628-70-7P

132628-71-8P 143314-86-7P 143314-87-8P

143874-46-8P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, as intermediate for duocarmycins or

pyrindamycins)

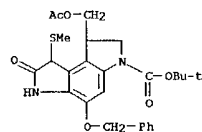
RN 132628-61-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,

1-[(acetyloxy)methyl]-

1,6,7,8-tetrahydro-8-(methylthio)-7-oxo-5-(phenylmethoxy)-,

1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 132628-62-7 CAPLUS

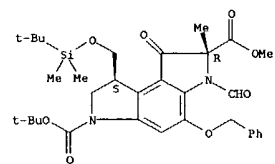
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,

1-[(acetyloxy)methyl]-

1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl

ester (9CI) (CA INDEX NAME)

L14 ANSWER 88 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 132628-68-3 CAPLUS

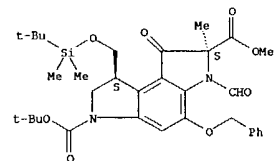
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,

8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-

tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)

2-methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 132628-70-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,

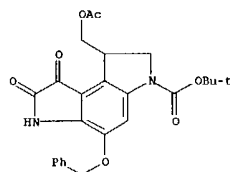
1,2,3,6,7,8-hexahydro-8-

(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-

indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L14 ANSWER 88 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

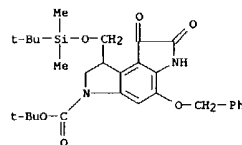


RN 132628-63-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[[[(1,1-

dimethylethyl)dimethylsilyl]oxy]methyl]-1,6,7,8-tetrahydro-7,8-dioxo-5-

(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 132628-67-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,

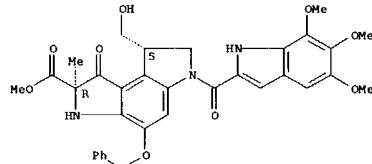
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-

tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)

2-methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L14 ANSWER 88 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 132628-71-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,

1,2,3,6,7,8-hexahydro-2-

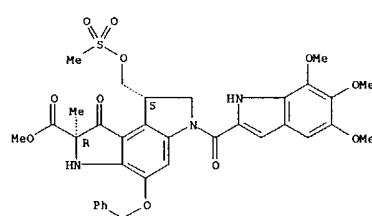
methyl-8-[[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-

trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA

INDEX

NAME)

Relative stereochemistry.



RN 143314-86-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,

1,2,3,6,7,8-hexahydro-2-

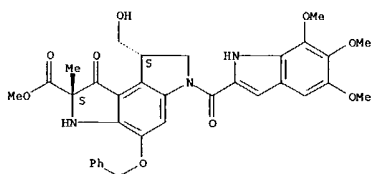
(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-

indol-2-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

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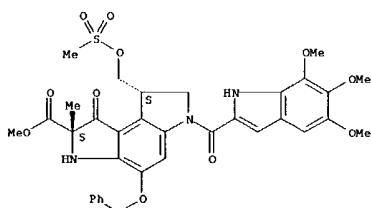
L14 ANSWER 88 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 143314-87-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
 1,2,3,6,7,8-hexahydro-2-

methyl 8-[[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

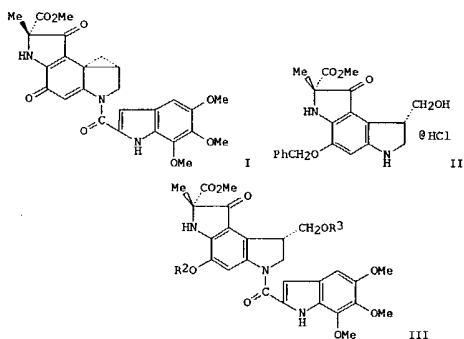
Relative stereochemistry.



RN 143874-46-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
 1,6,7,8-tetrahydro-1-(hydroxymethyl)-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester  
 (9CI) (CA INDEX NAME)

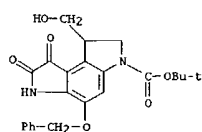
L14 ANSWER 89 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1992:591589 CAPLUS  
 DN 117:191589  
 TI Preparation of 2-epiduoarmycin A as antitumor agent  
 IN Terajima, Atsuro; Fukuda, Yasumichi; Nakatani, Kazuhiko; Ito, Yoshio  
 PA Zaidan Hojin Sagami Chuo Kagaku Kenkyusho, Japan  
 SO Jpn. Kokai Tokkyo Koho, 24 pp.  
 CODEN: JKKXAF  
 DT Patent  
 LA Japanese  
 FAN.CMT 1  

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04099774	A2	19920331	JP 1990-213741	19900814
PRAI JP 1990-213741		19900814		
OS MARPAT 117:191589				
GI				

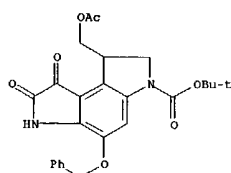


AB 2-Epiduoarmycin A (I) and its intermediates are prepared  
 Condensation of  
 (2S,8S)-II with 6,7,8-trimethoxy-1H-indole-2-carboxylic acid and  
 1-(3-dimethylaminopropyl)ethylcarbodiimide HCl in DMF gave 62%  
 indolyl  
 derivative (2S,8S)-III (R2 = PhCH2, R3 = H), which was mesylated  
 with MeSO2Cl  
 in CH2Cl2 to give 99% mesylate (2S,8S)-III (R2 = PhCH2, R3 = MeSO2)  
 (IV).

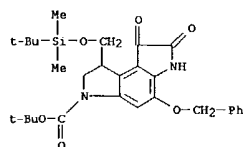
L14 ANSWER 88 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 89 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 Hydrogenolysis of IV over 10% Pd-C gave 83% phenolic deriv.  
 (2S,8S)-III  
 in (R2 = H, R3 = MeSO2), which was treated with NaH (50% oil dispersion)  
 in THF with stirring at room temp. to give 56% (DL)-I, which showed IC50  
 of 1.7 + 10-4 µg/mL against P-388 leukemic cells.  
 IT 132628-62-7P 132628-63-8P 132628-67-2P  
 132628-68-3P 132628-70-7P 132628-71-8P  
 143314-86-7P 143314-87-8P 143874-46-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (preparation and reaction of, in preparation of antitumor agent)  
 RN 132628-62-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
 1-[(acetyloxy)methyl]-  
 1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl  
 ester  
 (9CI) (CA INDEX NAME)



RN 132628-63-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

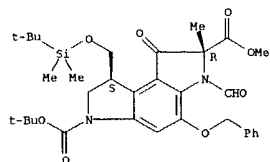


RN 132628-67-2 CAPLUS

10/069,202

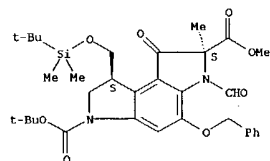
L14 ANSWER 89 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,  
 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-  
 tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)  
 2-methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 132628-68-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,  
 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-  
 tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)  
 2-methyl ester, cis- (9CI) (CA INDEX NAME)

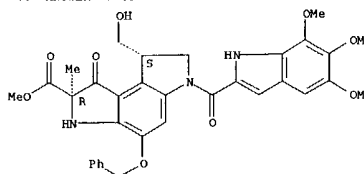
Relative stereochemistry.



RN 132628-70-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
 1,2,3,6,7,8-hexahydro-8-  
 (hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-  
 indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

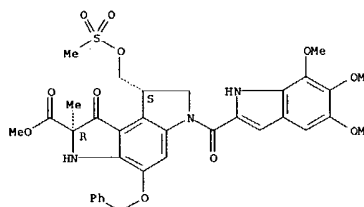
Relative stereochemistry.

L14 ANSWER 89 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 132628-71-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
 1,2,3,6,7,8-hexahydro-2-  
 methyl-8-[[[(methylsulfonyl)oxylmethyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-  
 trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA  
 INDEX NAME)

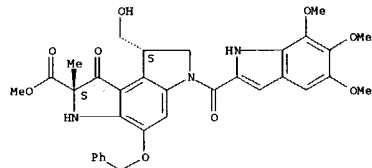
Relative stereochemistry.



RN 143314-86-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
 1,2,3,6,7,8-hexahydro-8-  
 (hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-  
 indol-2-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

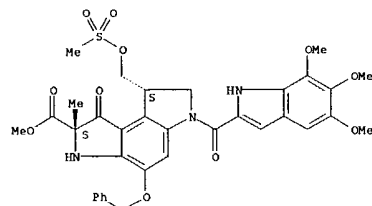
Relative stereochemistry.

L14 ANSWER 89 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



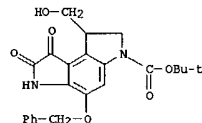
RN 143314-87-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
 1,2,3,6,7,8-hexahydro-2-  
 methyl-8-[[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-  
 trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, cis- (9CI) (CA  
 INDEX NAME)

Relative stereochemistry.



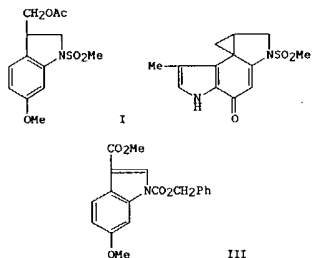
RN 143874-46-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
 1,6,7,8-tetrahydro-1-  
 (hydroxymethyl)-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester  
 (9CI) (CA INDEX NAME)

L14 ANSWER 89 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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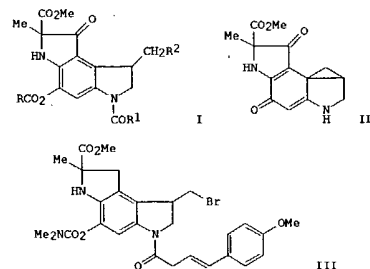
L14 ANSWER 90 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1992:194003 CAPLUS  
 DN 116:194003  
 TI Tandem Michael addition-[3,3]sigmatropic rearrangement processes.  
 Part 2.  
 of Construction of cyclopropa[3,4]pyrrolo[3,2-e]indol-4-one (CPI) unit  
 of antitumor antibiotic CC-1065  
 AU Toyota, Masahiro; Fukumoto, Keiichiro  
 CS Pharm. Inst., Tohoku Univ., Sendai, 980, Japan  
 SO Journal of the Chemical Society, Perkin Transactions 1: Organic and  
 Bio-Organic Chemistry (1972-1999) (1992), (5), 547-52  
 CODEN: JCPRB4; ISSN: 0300-922X  
 DT Journal  
 LA English  
 GI



AB Development of an alternative strategy for preparing  
 3-acetoxymethyl-2,3-  
 dihydro-1-methylsulfonyl-6-methoxyindole (I) has been completed.  
 Since I  
 was an intermediate in a previous synthesis of the CPI unit (II) of  
 CC-1065, this achievement constitutes a formal synthesis of racemic  
 II.  
 The key strategic element of the approach involves the tandem Michael  
 addition-[3,3]sigmatropic rearrangement process of HC.tplbond.CO2Me  
 and  
 3-MeOC6H4N(OH)CO2CH2Ph, prepared from 3-O2NC6H4OMe, to furnish  
 indole III as  
 the sole product. Subsequent elaboration of III into I was then  
 achieved

L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1992:106269 CAPLUS  
 DN 116:106269  
 TI Preparation of DC-89 derivatives as neoplasm inhibitors  
 IN Saito, Hiromitsu; Asai, Akira; Nagamura, Satoru; Kobayashi, Eiichi;  
 Gomi, Katsushige  
 PA Kyowa Hakko Kogyo Co., Ltd., Japan  
 SO Eur. Pat. Appl., 25 pp.  
 CODEN: EPXKDW  
 DT Patent  
 LA English  
 FAN.CNT 1

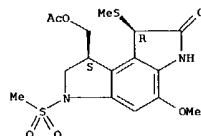
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 461603	A1	19911218	EP 1991-109533	19910611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5214065	A	19930525	US 1991-710407	19910605
JP 04226988	A2	19920817	JP 1991-137741	19910610
US 5248692	A	19930928	US 1993-24472	19930301
PRAI JP 1990-152098		19900611		
US 1991-710407		19910605		
OS MARPAT 116:106269				
GI				



AB Title compds. [I: R = amino, morpholino, pyrrolidinyl, piperidinyl,  
 homopiperidinyl, etc.; R1 = (substituted) phenylethenyl,  
 phenoxyethyl,  
 acylaminoindolyl, etc.; R2 = Cl, Br], were prepared Thus,  
 antibiotic DC-89A  
 was stirred with NaOMe in MeOH to give 97% intermediate II. II was  
 acylated with p-nitrophenyl 4-methoxycinnamate/NaH and the product  
 was

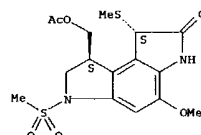
L14 ANSWER 90 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 by applying M. P. Cava et al's (1989) technique. The conversion of I  
 into  
 II was also achieved with the method of W. Wierenga (1981).  
 IT 140862-50-6P 140862-51-7P  
 RN 140862-50-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrol-2(1H)-one, 8-[(acetyloxy)methyl]-3,6,7,8-  
 tetrahydro-4-methoxy-6-(methylsulfonyl)-1-(methylthio)-, cis- (9CI)  
 (CA INDEX NAME)

Relative stereochemistry.

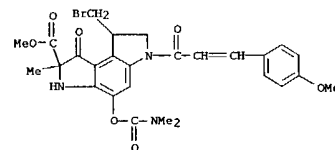


RN 140862-51-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrol-2(1H)-one, 8-[(acetyloxy)methyl]-3,6,7,8-  
 tetrahydro-4-methoxy-6-(methylsulfonyl)-1-(methylthio)-, trans- (9CI)  
 (CA INDEX NAME)

Relative stereochemistry.



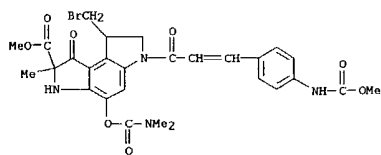
L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 treated with aq. HBr and then Me2NCOCl to give title compd. III. III  
 at  
 16 mg/kg i.v. in mice reduced the size of sarcoma 180 tumors to 7.8%  
 of  
 controls.  
 IT 139147-43-6P 139147-44-7P 139147-45-8P  
 139147-46-9P 139147-47-0P 139147-48-1P  
 139147-49-2P 139147-50-5P 139147-51-6P  
 139147-52-7P 139147-53-8P 139147-54-9P  
 139147-55-0P 139147-56-1P 139147-57-2P  
 139147-58-3P 139147-59-4P  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological  
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic  
 use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of, as neoplasm inhibitor)  
 RN 139147-43-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-  
 [(dimethylamino)carbonyloxy]-1,2,3,6,7,8-hexahydro-6-[3-(4-  
 methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-1-oxo-, methyl ester (9CI)  
 (CA INDEX NAME)



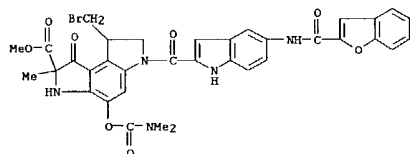
RN 139147-44-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-  
 [(dimethylamino)carbonyloxy]-1,2,3,6,7,8-hexahydro-6-[3-(4-  
 methoxycarbonyl)amino]phenyl]-1-oxo-2-propenyl]-2-methyl-1-oxo-,  
 methyl  
 ester (9CI) (CA INDEX NAME)

10/069,202

L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

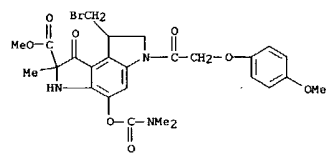


RN 139147-45-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(bromomethyl)-4-[[dimethylamino]carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

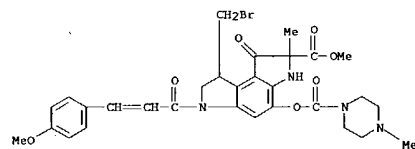


RN 139147-46-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-6-[[5-[(2,4-dimethoxyphenyl)-1-oxo-2,4-pentadienyl]-4-[[dimethylamino]carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

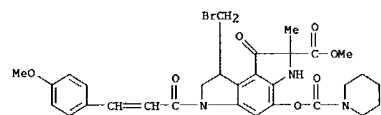
L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 139147-49-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

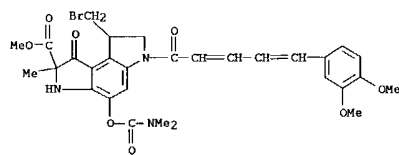


RN 139147-50-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-1-oxo-4-[[1-piperidinylcarbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

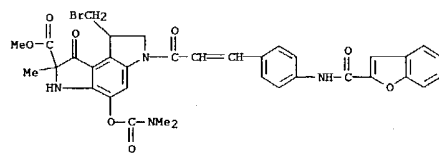


RN 139147-51-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-

L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

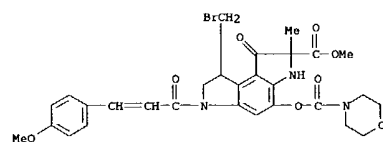


RN 139147-47-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[3-[(2-benzofuranylcarbonyl)amino]phenyl]-1-oxo-2-propenyl]-8-(bromomethyl)-4-[[dimethylamino]carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

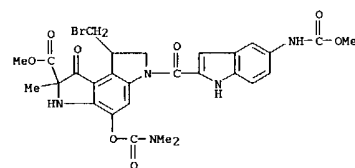


RN 139147-48-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[dimethylamino]carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[[4-methoxyphenoxy]acetyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



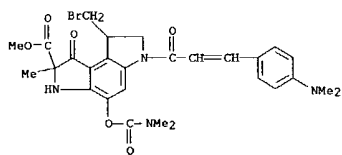
RN 139147-52-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[dimethylamino]carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[[5-[(methoxycarbonyl)amino]-1H-indol-2-yl]carbonyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



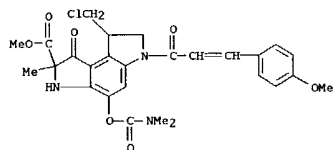
RN 139147-53-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[dimethylamino]carbonyl]oxy]-6-[3-[(4-dimethylamino)phenyl]-1-oxo-2-propenyl]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

10/069,202

L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

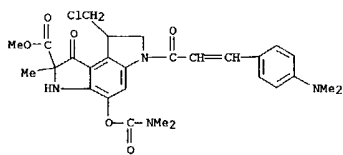


RN 139147-54-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-4-[[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-1-oxo-, methyl ester (9CI)  
(CA INDEX NAME)

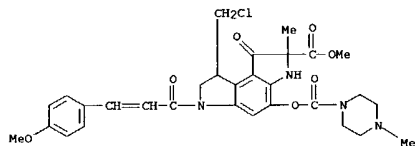


RN 139147-55-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-4-[[[(dimethylamino)carbonyl]oxy]-6-[3-(4-(dimethylamino)phenyl)-1-oxo-2-propenyl]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-, methyl ester (9CI)  
(CA INDEX NAME)

L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

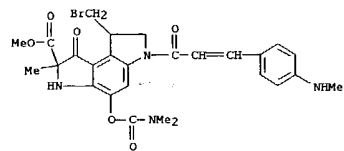


RN 139147-56-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-, methyl ester (9CI)  
(CA INDEX NAME)

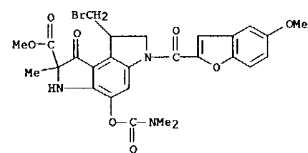


RN 139147-57-2 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-6-[3-(4-(methylamino)phenyl)-1-oxo-2-propenyl]-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

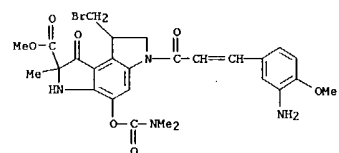
L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 139147-58-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[15-methoxy-2-benzofuranyl]carbonyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 139147-59-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[3-(3-amino-4-methoxyphenyl)-1-oxo-2-propenyl]-8-(bromomethyl)-4-[[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo- (9CI)  
(CA INDEX NAME)



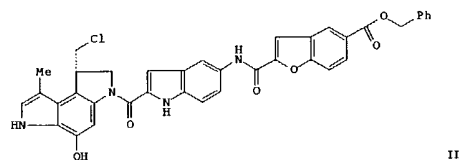
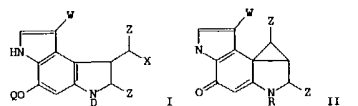
L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



10/069,202

L14 ANSWER 92 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1992:83450 CAPLUS  
 UN 116:83450  
 TI Preparation of CC-1065 analogs as neoplasm inhibitors.  
 IN Acistoff, Paul Adrian; Kelly, Robert Charles; Mitchell, Mark Allen  
 PA Upjohn Co., USA  
 SO PCT Int. Appl., 119 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1  
 PATENT NO. KIND DATE APPLICATION NO. DATE  
 -----  
 PI WO 9116324 A1 19911031 WO 1991-US2704 19910424  
 W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO,  
 PL, RO, SD, SU, US  
 RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR,  
 IT, LU, ML, MR, NL, SE, SN, TD, TG  
 CA 2078118 AA 19911026 CA 1991-2078118 19910424  
 CA 2078118 C 19911116  
 AU 9177954 A1 19911111 AU 1991-77954 19910424  
 AU 648313 B2 19940421  
 EP 527189 A1 19930217 EP 1991-909127 19910424  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE  
 JP 05508394 T2 19931125 JP 1991-508837 19910424  
 US 5739350 A 19980414 US 1995-479231 19950607  
 PRAI US 1990-513501 A2  
 WO 1991-US2704 A 19910424  
 US 1992-966139 B1 19921023  
 US 1994-279767 B1 19940725  
 OS MARPAT 116:83450  
 GI

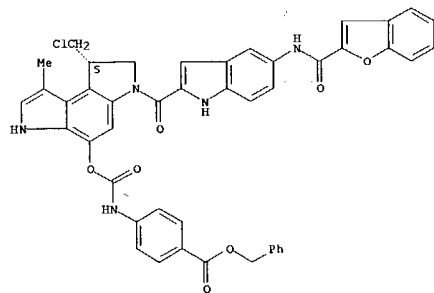
L14 ANSWER 92 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



AB Title compds. [I and II; W, Z = H, alkyl, Ph; X = halo, N3, (thio)cyanate, (thio)isocyanate, phosphate ester, sulfonyl, etc.; D, R = heteroarylacyl; Q = H, (thio)acyl, alkoxy or phenoxycarbonyl, (thio)carbamoyl, etc.], were prepared as synthetic intermediates and as neoplasm inhibitors. They may also be linked to monoclonal antibodies or human CD4 protein. Thus, title compound III was prepared from 1,1-dimethylethyl S-1-chloromethyl-1,6-dihydro-5-hydroxy-8-methylbenzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylate and the corresponding benzimidazolecarboxylic acid derivative (preparation given) via deprotection of the benzodipyrrole and carbodiimide coupling. Title compds. at 0.1-0.4 mg/kg showed T/C = 133-200% against K1210 leukemia in mice.  
 IT 138730-88-8P 138730-91-3P 138730-94-6P  
 138731-06-3P 138731-08-5P 138731-09-6P  
 138731-11-0P  
 RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, as neoplasm inhibitor and intermediate)  
 RN 138730-88-8 CAPLUS  
 CN Benzoic acid, 4-[[[3-[[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-1-(chloromethyl)-1,2,3,6-tetrahydro-8-methylbenzo[1,2-b:4,3-b']dipyrrole-5-yl]oxy]carbonyl]amino]phenyl]-1-oxopropyl]-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

L14 ANSWER 92 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 b')dipyrrole-5-yl]oxy]carbonyl]amino]-, phenylmethyl ester, (S)- (9CI) (CA INDEX NAME)

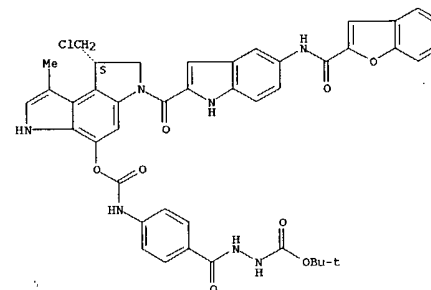
Absolute stereochemistry.



RN 138730-91-3 CAPLUS  
 CN Hydrazinecarboxylic acid, 2-[4-[[[3-[[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-1-(chloromethyl)-1,2,3,6-tetrahydro-8-methylbenzo[1,2-b:4,3-b']dipyrrole-5-yl]oxy]carbonyl]amino]benzoyl]-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 92 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

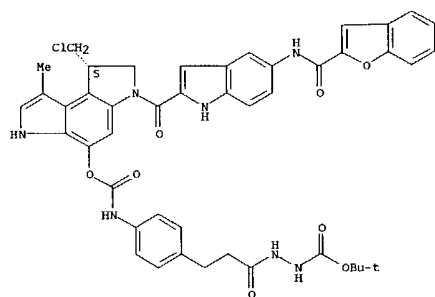


RN 138730-94-6 CAPLUS  
 CN Hydrazinecarboxylic acid, 2-[3-[4-[[[3-[[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-1-(chloromethyl)-1,2,3,6-tetrahydro-8-methylbenzo[1,2-b:4,3-b']dipyrrole-5-yl]oxy]carbonyl]amino]phenyl]-1-oxopropyl]-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/069,202

L14 ANSWER 92 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

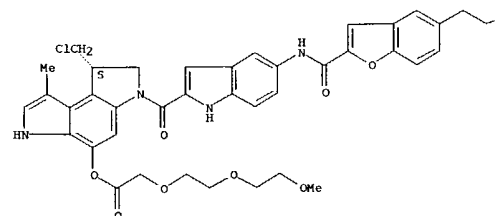


RN 138731-06-3 CAPLUS  
CN Hydrazinecarboxylic acid,  
2-[3-[2-[[[2-[[[1-(chloromethyl)-1,6-dihydro-5-  
[[[2-(2-methoxyethoxy)ethoxy]acetyl]oxy]-8-methylbenzo[1,2-b:4,3-  
b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-5-  
benzofuranyl]-1-oxopropyl]-, 1,1-dimethylethyl ester, (S)- (9CI) (CA  
INDEX NAME)

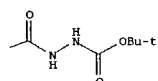
Absolute stereochemistry.

L14 ANSWER 92 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

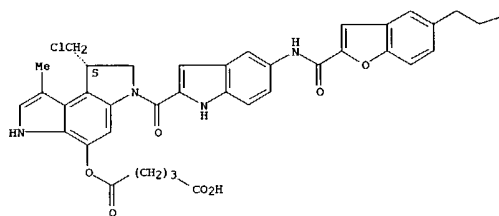


RN 138731-08-5 CAPLUS  
CN Pentanedioic acid, mono[1-(chloromethyl)-3-[[[5-[[[3-[2-[[[1,1-  
dimethylethoxy]carbonyl]hydrazino]-3-oxopropyl]-2-  
benzofuranyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1,2,3,6-tetrahydro-8-  
methylbenzo[1,2-b:4,3-b']dipyrrol-5-yl] ester, (S)- (9CI) (CA INDEX  
NAME)

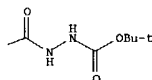
Absolute stereochemistry.

L14 ANSWER 92 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

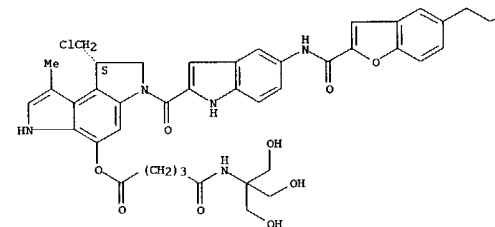


RN 138731-09-6 CAPLUS  
CN Hydrazinecarboxylic acid,  
2-[3-[2-[[[2-[[[1-(chloromethyl)-1,6-dihydro-5-  
[[[5-[[[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]amino]-1,5-dioxopentyl]oxy]-8-  
methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-  
yl]amino]carbonyl]-5-benzofuranyl]-1-oxopropyl]-, 1,1-dimethylethyl  
ester, (S)- (9CI) (CA INDEX NAME)

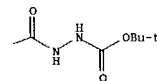
Absolute stereochemistry.

L14 ANSWER 92 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



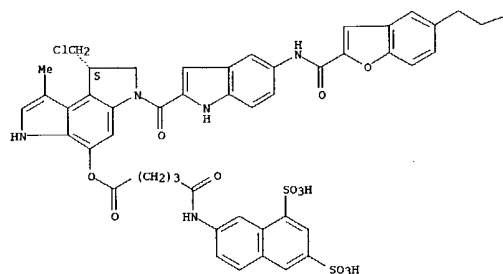
RN 138731-11-0 CAPLUS  
CN Hydrazinecarboxylic acid, 2-[3-[2-[[[2-[[[1-(chloromethyl)-5-[[[5-[[[6,8-  
disulfo-2-naphthalenyl]amino]-1,5-dioxopentyl]oxy]-1,6-dihydro-8-  
methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-  
yl]amino]carbonyl]-5-benzofuranyl]oxopropyl]-, 1,1-dimethylethyl  
ester,  
disodium salt, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

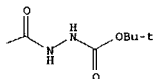
10/069,202

L14 ANSWER 92 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



● 2 Na

L14 ANSWER 93 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

AB The antibiotics SF2582 A (I), B, and C (II), also useful as neoplasm inhibitors, are manufactured by culture of Streptomyces. Derivs. of the antibiotics having improved antitumor activities are prepared Streptomyces SF2582 was shake-cultured for 5 days at 28°, and the cell mass from 1000 L culture broth recovered by filtration. I, antibiotic SF2582B, and II 182, 88, and 450 mg, resp., were recovered from the cell mass by extraction and chromatog. The sulfate or alkyl- or arylsulfonate derivs. (4) were prepared from II and their antitumor activity determined Against P388 cells, the derivs. had LC50 (ng/mL) of 4-2500, as compared to 9400 for II. Also given was the morphol. and physiol. characteristics of Streptomyces SF2582. The physicochem. characteristics of I, SF2582B, and II were also given.

IT 126590-90-7P 136483-61-9P 136483-62-0P  
136772-69-5P

RL: PREP (Preparation)

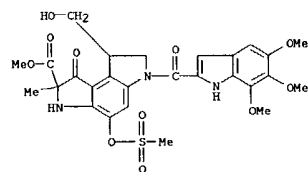
(preparation of, from antibiotic SF2582C, enhanced antitumor activity of)

RN 126590-90-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,

1,2,3,6,7,8-hexahydro-8-

(hydroxymethyl)-2-methyl-4-[(methylsulfonyl)oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 136483-61-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,

1,2,3,6,7,8-hexahydro-2-

methyl-4-[(methylsulfonyl)oxy]-8-[(methylsulfonyl)oxymethyl]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 93 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1992:19720 CAPLUS

DN 116:19720

TI Antibiotics SF2582 manufacture with Streptomyces

IN Ohba, Kazunori; Watabe, Hiroomi; Nagasawa, Mieko; Sakakibara, Shiro; Shomura, Takashi; Sezaki, Masaji; Kondo, Shinichi; Koyama, Masao; Nakazawa, Tadashi; Yamamoto, Haruo

PA Meiji Seika Kaisha, Ltd., Japan

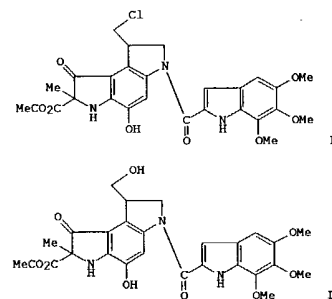
SO U.S., 20 pp. Cont.-in-part of U.S. Ser. No. 276,714, abandoned.  
CODEN: USXXAM

DT Patent

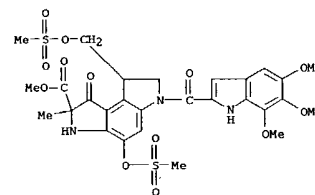
LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4994578	A	19910219	US 1989-344738	19890428
	JP 01139590	A2	19890601	JP 1987-297476	19871127
	JP 01265890	A2	19891023	JP 1988-94544	19880419
	JP 01275581	A2	19891106	JP 1988-103782	19880428
	JP 2562935	B2	19961211		
PRAI	US 5037993	A	19910806	US 1990-520424	19900508
	JP 1987-297476		19871127		
	JP 1988-94544		19880419		
	JP 1988-103782		19880428		
	US 1988-276714		19881128		
GI	US 1989-344738		19890428		



L14 ANSWER 93 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

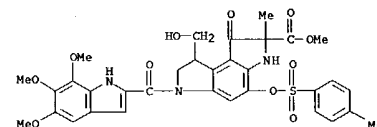


RN 136483-62-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,

1,2,3,6,7,8-hexahydro-8-

(hydroxymethyl)-2-methyl-4-[(4-methylphenyl)sulfonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 136772-69-5 CAPLUS

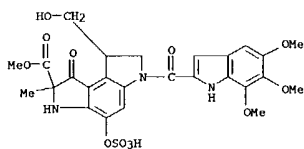
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,

1,2,3,6,7,8-hexahydro-8-

(hydroxymethyl)-2-methyl-1-oxo-4-(sulfoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

10/069,202

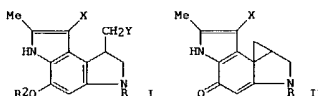
L14 ANSWER 93 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



MeO  
HO-CH<sub>2</sub>  
Me  
HN  
OS<sub>3</sub>H  
Me  
HN  
MeO  
MeO  
MeO

L14 ANSWER 94 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1991:408427 CAPLUS  
DN 115:8427  
TI Preparation of DC-88A derivatives as antitumor agents  
IN Kanda, Yutaka; Uosaki, Youichi; Saito, Hiromitsu; Sano, Hiroshi;  
Kobayashi, Eiji; Morimoto, Makoto; Nagamura, Satoru  
PA Kyowa Hakko Kogyo Co., Ltd., Japan  
SO Eur. Pat. Appl., 29 pp.  
CODEN: EPXXDW  
DT Patent  
LA English  
FAN.CW 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 406749	A1	19910109	EP 1990-112563	19900702
EP 406749	B1	19991027		
R: DE, FR, GB, IT				
JP 03128379	A2	19910531	JP 1990-168666	19900627
JP 2510335	B2	19960626		
US 5070092	A	19911203	US 1990-545579	19900629
US 5187186	A	19930216	US 1991-755760	19910906
PRAI JP 1989-171605		19890703		
US 1990-545579		19900629		
MARFAT 115:8427				
OS				
GI				

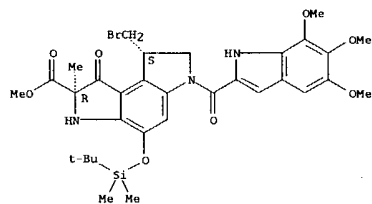


AB The title compds. (I and II; R = 5,6,7-trimethoxy-2-indolylcarbonyl;  
R2 = H, alkanoyl, dialkylcarbamoyl, alkoxy-carbonyl, trialkylsilyl, etc.; X  
= H, CO2R1; R1 = H, alkyl, allyl, PhCH2; Y = Cl, Br) were prepared Thus,  
DC89B2 (fermentation preparation given) was converted in 3 steps to I (R2 =  
SiMe2OMe3, X = CO2Me, Y = Br) which suppressed Sarcoma 180 tumor growth in mice to  
4.3 volume% that of controls 7 days after administration of 0.25 mg/kg  
i.v.  
IT 129953-15-7P 134106-83-5P 134106-84-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT (Reactant or reagent)

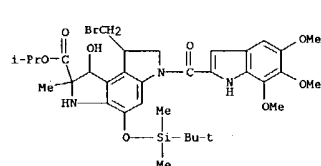
L14 ANSWER 94 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

(prepn. and reaction of, in prepn. of antitumor agents)  
RN 129953-15-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-  
dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-  
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-  
(9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

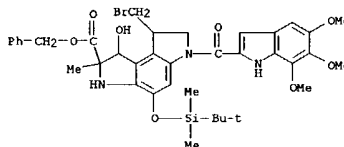


RN 134106-83-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-  
dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-  
6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methylethyl ester  
(9CI)  
(CA INDEX NAME)

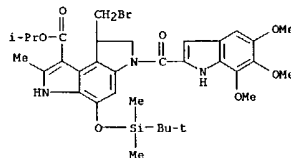


RN 134106-84-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-  
dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-  
6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methylethyl ester  
(9CI)  
(CA INDEX NAME)

L14 ANSWER 94 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, phenylmethyl ester  
(9CI)  
(CA INDEX NAME)

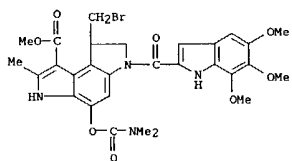


IT 134106-73-3P 134106-75-5P 134106-76-6P  
134106-77-7P 134106-78-8P 134106-79-9P  
134106-80-2P 134106-81-3P 134106-82-4P  
134127-18-7P 134127-20-1P  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(preparation of, as antitumor agent)  
RN 134106-73-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-  
dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methylethyl ester (9CI) (CA  
INDEX NAME)



RN 134106-75-5 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-  
[[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-  
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX  
NAME)

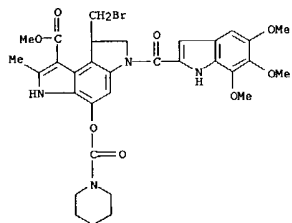
L14 ANSWER 94 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 134106-76-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[(1-piperidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

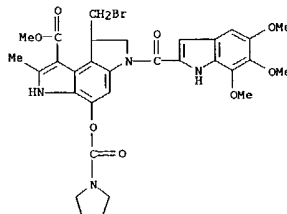


RN 134106-77-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[(1-pyrrolidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

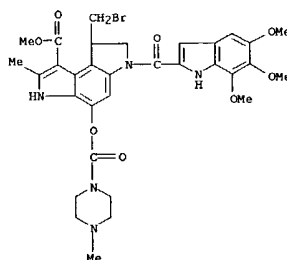
L14 ANSWER 94 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 134106-78-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

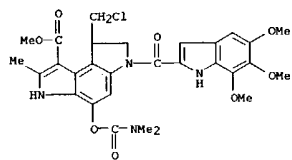
tetrahydro-2-methyl-4-[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 134106-79-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

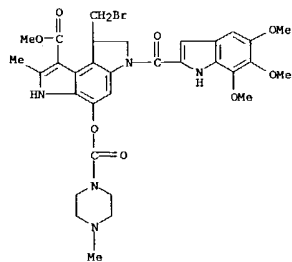
L14 ANSWER 94 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 134106-80-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



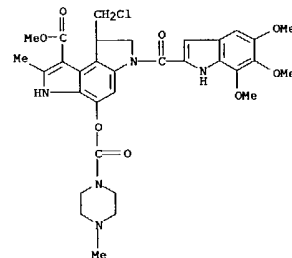
● HCl

RN 134106-81-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

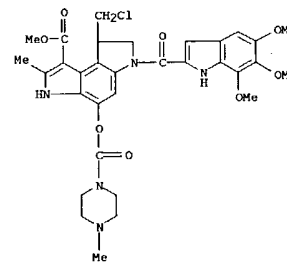
L14 ANSWER 94 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 134106-82-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(chloromethyl)-3,6,7,8-

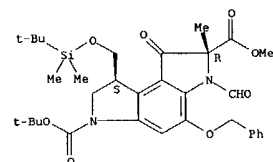
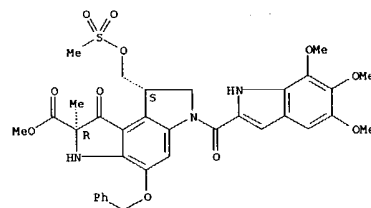
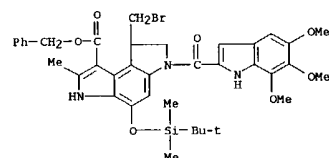
tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

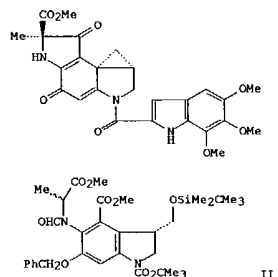
RN 134127-18-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-



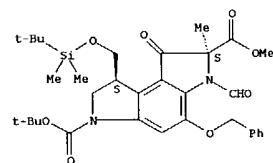
RN 132628-68-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrrole-2,6(1H)-dicarboxylic acid,  
8-[[{[1,1-dimethylethyl]dimethylsilyl}oxy]methyl]-3-formyl-2,3,7,8-  
tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)-  
2-methyl ester, cis- (9CI) (CA INDEX NAME)

L14 ANSWER 95 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1991:142962 CAPLUS  
DN 114:142962  
TI First total synthesis of dl-duocarmycin A  
AU Fukuda, Yasumichi; Nakatani, Kazuhiko; Ito, Yoshio; Terashima, Shiro  
CA Chem. Res. Cent., Sagamihara, 229, Japan  
SO Tetrahedron Letters (1990), 31(46), 6699-9  
CODEN: TELEAY; ISSN: 0040-4039  
DT Journal  
LA English  
OS CASREACT 114:142962  
GI



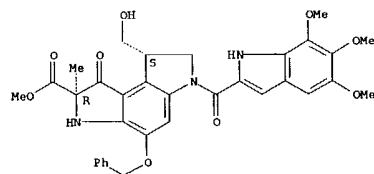
AB Synthesis of the title compound (I) was achieved by featuring  
introduction  
of a methoxycarbonyl group into the C-4 position of a 5-amindoline  
nucleus by way of an isatin derivative and subsequent ring closure to  
a Me  
2-methylindoxyl-2-carboxylate system by the Dieckmann cyclization the  
indolylformamide II.  
IT 132628-71-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT  
(Reactant or reagent)  
(preparation and hydrogenolysis of)  
RN 132628-71-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
1,2,3,6,7,8-hexahydro-2-  
methyl-8-[[ (methylsulfonyl)oxy]methyl]-1-oxo-4- (phenylmethoxy)-6-[[5,6,7-

L14 ANSWER 95 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
Relative stereochemistry.



IT 132628-70-7F  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT  
 (Reactant or reagent)  
 (preparation and mesylation of)  
 RN 132628-70-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
 1,2,3,6,7,8-hexahydro-8-  
 (hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-  
 indol-2-yl)]carbonyl-, methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



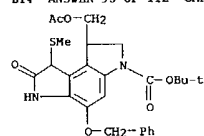
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IT      132628-61-6P 132628-63-8P
Rl: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACl:
(Reactant or reagent)
      (Preparation and oxidation of)
CN      132628-61-6 CAPLUS
RN      Benzof[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,
1-[1-(acetylthio)methyl]-
1,6,8-trisubstituted-9-(methylthio)-7-oxo-5-(phenylmethoxy)-,
1,1-dimethylthio ester (9CI) (CA INDEX NAME)

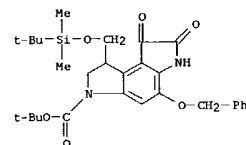
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10/069,202

L14 ANSWER 95 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 132628-63-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

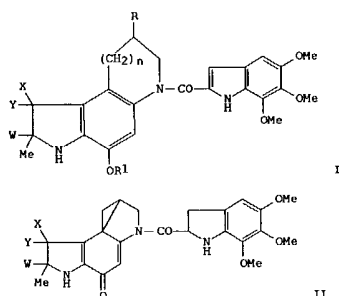


IT 132628-62-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (preparation and silylation of)  
 RN 132628-62-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
 1-[(acetyloxy)methyl]-  
 1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl  
 ester  
 (9CI) (CA INDEX NAME)

L14 ANSWER 96 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

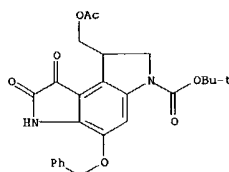
AN 1990:591321 CAPLUS  
 DN 113:191321  
 TI Preparation of DC-88A derivatives as antitumor agents  
 IN Kanda, Yutaka; Yasuzawa, Tokuo; Saito, Hiromitsu; Sano, Hiroshi;  
 Kobayashi, Eiji; Morimoto, Makoto  
 PA Kyowa Hakko Kogyo Co., Ltd., Japan  
 SO Eur. Pat. Appl., 39 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 365041	A1	19900425	EP 1989-119639	19891023
EP 365041	B1	19951004		
R: DE, FR, GB, IT				
US 5008271	A	19910416	US 1989-423788	19891018
JP 03007287	A2	19910114	JP 1989-272314	19891019
FRAI JP 1989-265582		19891021		
JP 1989-62572		19890315		
OS MARPAT 113:191321				
GI				



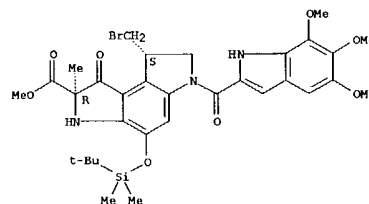
AB DC-88A derivs. [I, II; R = Br, Cl, BrCH<sub>2</sub>, ClCH<sub>2</sub>; R<sub>1</sub> = H, Cl-4 alkyl,  
 C2-15  
 acyl, (substituted) benzoyl, dialkylcarbonyl, etc.; one of X and Y  
 is H,  
 the other is MeO, AcO, (substituted) PhCO<sub>2</sub>, XY = O, W = H, allyl,  
 (substituted) acyl, alkoxycarbonyl, alkoxymethyl, etc.; n = 0, 1] are

L14 ANSWER 95 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 96 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 prepd. Me<sub>3</sub>CSiMe<sub>2</sub>Cl was added to a soln. of DC-89B2 (I; R = BrCH<sub>2</sub>, R<sub>1</sub> = H,  
 W = CO<sub>2</sub>Me, XY = O, n = 0) (prepn. by culture fermn. given) and  
 imidazole  
 in DMF at 0° with stirring. 2N HCl was added, and the mixt. extd.  
 with EtOAc to give 95% silyl ether I (R = BrCH<sub>2</sub>, R<sub>1</sub> = Me<sub>3</sub>CSiMe<sub>2</sub>, W =  
 CO<sub>2</sub>Me, XY = O, n = 0), which showed IC<sub>50</sub> of 0.010 nM against HeLa S3  
 Cell  
 growth, vs. 0.039 nM with DC-88A. Also prepd. were 32 addnl. I and  
 II.  
 IT 129953-15-7P 129953-16-8P 129953-17-9P  
 129953-19-1P 129953-20-4P 129953-21-5P  
 129953-22-6P 129953-23-7P 129953-24-8P  
 129953-25-9P 129953-26-0P 129953-28-2P  
 129953-32-8P 129982-35-0P  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological  
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic  
 use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of, as antitumor agent)  
 RN 129953-15-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
 8-(bromomethyl)-4-[[[(1,1-  
 dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-  
 [(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-  
 (9CI)  
 (CA INDEX NAME)

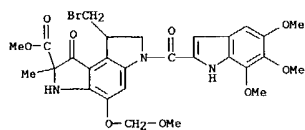
Absolute stereochemistry.



RN 129953-16-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-  
 1,2,3,6,7,8-hexahydro-4-(methoxymethoxy)-2-methyl-1-oxo-6-[(5,6,7-  
 trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX  
 NAME)

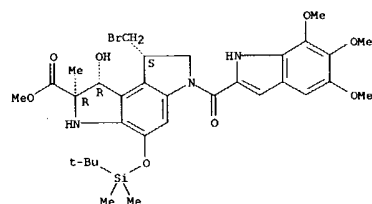
10/069,202

L14 ANSWER 96 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 129953-17-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R,2R,8S)- (9CI) (CA INDEX NAME)

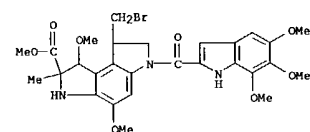
Absolute stereochemistry.



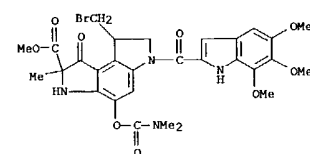
RN 129953-19-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 96 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 129953-22-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1,4-dimethoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

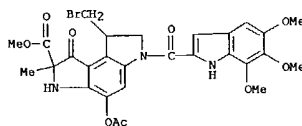


RN 129953-23-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

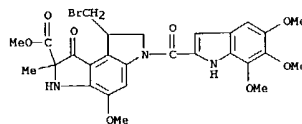


RN 129953-24-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[(2-propenyloxy)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 96 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

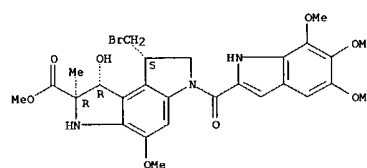


RN 129953-20-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-methoxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

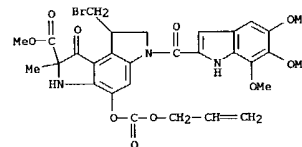


RN 129953-21-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1-hydroxy-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R-(1a,2p,8a))- (9CI) (CA INDEX NAME)

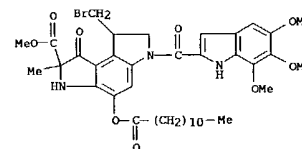
Absolute stereochemistry. Rotation (-).



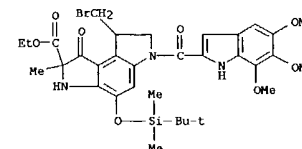
L14 ANSWER 96 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 129953-25-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[(1-oxododecyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 129953-26-0 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

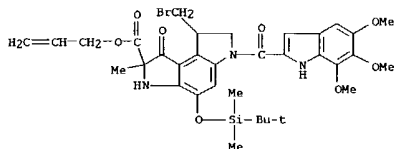




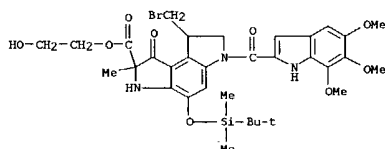
10/069,202

L14 ANSWER 96 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 129953-28-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-  
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester (9CI)  
(CA INDEX NAME)

RN 129953-32-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,  
8-(bromomethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-  
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-hydroxyethyl ester  
(9CI)  
(CA INDEX NAME)

RN 129982-35-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1-(acetyloxy)-8-  
(bromomethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-  
hexahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,  
methyl

L14 ANSWER 97 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1990:552387 CAPLUS

DN 113:152387

TI GC-1065 analogs having two CPI subunits useful as antitumor agents  
and

ultraviolet light absorbers

IN Kelly, Robert C.; Aristoff, Paul A.

PA Upjohn Co., USA

SO Eur. Pat. Appl., 49 pp.

CODEN: EPKXDW

DT Patent

LA English

FAN.CMT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 359454	A1	19900321	EP 1989-308920	19890904
EP 359454	B1	20001227		
WO 9002746	A1	19900322	WO 1989-US3329	19890807
W: AU, DK, FI, HU, JP, KR, NO, SU, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8941922	A1	19900402	AU 1989-41922	19890807
AU 632288	B2	19921224		
JP 04500664	T2	19920206	JP 1989-509236	19890807
JP 3380237	B2	20030224		
CA 1340215	A1	19981215	CA 1989-608908	19890821
AT 198335	E	20010115	AT 1989-308920	19890904
ES 2153814	T3	20010316	ES 1989-308920	19890904
KR 137959	B1	19980515	KR 1990-700977	19900511
DK 9100417	A	19910308	DK 1991-417	19910308
US 5541339	A	19960730	US 1991-659415	19910308
NO 9100958	A	19910510	NO 1991-958	19910311
GR 3035589	T3	20010629	GR 2001-400433	20010315
LV 12806	B	20020520	LV 2001-180	20011227
PRAI US 1988-243350	A	19880912		
WO 1989-US3329	A	19890807		

OS MARPAT 113:152387

G1 For diagram(s), see printed CA Issue.

AB CPI1-R5-T-R6-CPI2 [CPI1, CPI2 = Q, Q1; W = alkyl, pH, H; C = N3,  
halo,

cyanato, thiocyanato, isocyanato, thioisocyanato, P(O) (OR)2, etc.; Y

C(O)R, C(S)R, C(O)OE1, C(O)NR2R3, etc.; Z = alkyl, alkenyl, alkynyl,  
(substituted) Ph, etc.; R1 = alkyl, (substituted) phenyl; R2, R3 = H,  
alkyl, (substituted) Ph, etc.; T = NHCO, CONH, C(O)O, OC(O), etc.;

R5, R6

= bond, acyl etc.), useful as antitumors and UV absorbers in textile  
industry, were prepared Indole derivative I (R7 = OH) (preparation  
given)

condensed with benzodipyrrole derivative Q2CO2Me3 to give I (R7 =

Q2).

This at 15 µg/kg i.v. effected 60% cure (surviving 30 days) in mice

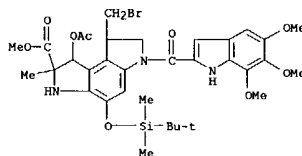
transplanted with L 1210 leukemia cells.

IT 129655-29-4P 129655-34-1P 129655-35-2P

RL: SPN (Synthetic preparation); PREF (Preparation)

(preparation of, as antitumor and UV absorber)

RN 129655-29-4 CAPLUS

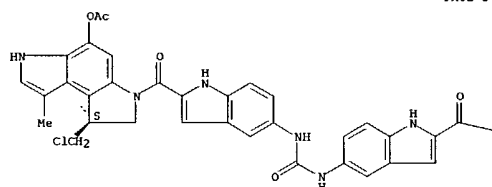
L14 ANSWER 96 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
ester (9CI) (CA INDEX NAME)

L14 ANSWER 97 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

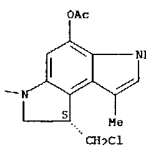
CN Benzo[1,2-b:4,3-b']dipyrrole-4-ol,  
6,6'-[carbonylbis(imino-1H-indole-5,2-  
diylcarbonyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-1-methyl-  
diacetate  
(ester), [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RN 129655-34-1 CAPLUS

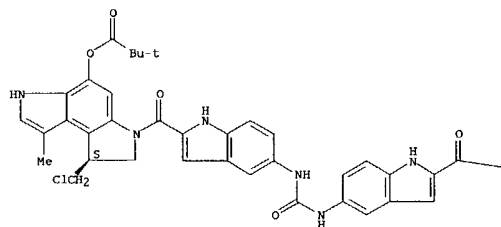
CN Propanoic acid, 2,2-dimethyl-, carbonylbis[imino-1H-indole-5,2-  
diylcarbonyl][1-(chloromethyl)-1,6-dihydro-8-methylbenzo[1,2-b:4,3-  
b']dipyrrole-3,5(2H)-diyl] ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

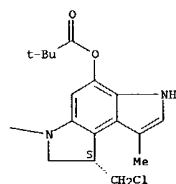
10/069,202

L14 ANSWER 97 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



RN 129655-35-2 CAPLUS  
 CN Decanoic acid, carbonylbis[imino-1H-indole-5,2-diylcarbonyl[1-(chloromethyl)-1,6-dihydro-8-methylbenzo[1,2-b:4,3-b']dipyrrole-3,5(2H)-diyl]] ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

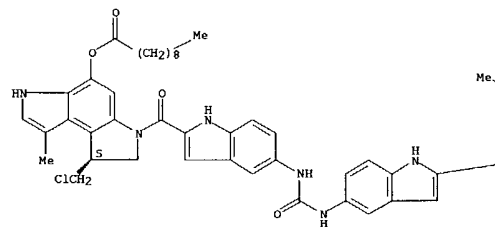
Absolute stereochemistry.

L14 ANSWER 98 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1990:531891 CAPLUS  
 DN 113:131891  
 TI Analogs of antibiotic CC-1065, namely 1,2,8,8a-tetrahydrocyclopropa[c]pyrrolo[3,2-e]indol-4-(5H)-ones and related compounds with light-absorbing, antibacterial, and antitumor activities  
 IN Kelly, Robert C.; Warpehoski, Martha A.; Wierenga, Wendell  
 PA Upjohn Co., USA  
 SO U.S., 53 pp. Cont.-in-part of U.S. Ser. No. 694,363, abandoned.  
 DT Patent  
 LA English  
 FAN.CNT 2

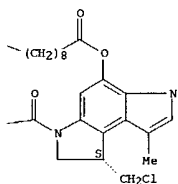
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 4912227	A	19900327	US 1986-894314	19860807
CA 1238907	A1	19880705	CA 1985-473917	19850208
ZA 8501093	A	19850925	ZA 1985-1093	19850213
EP 154445	A1	19850911	EP 1985-301125	19850220
EP 154445	B1	19890531		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
JP 60193989	A2	19851002	JP 1985-31662	19850221
JP 2545060	B2	19961016		
CA 1293248	A2	19911217	CA 1987-552543	19871123
US 4978757	A	19901218	US 1989-444176	19891130
PRAI US 1984-581836		19840221		
US 1985-694363		19850124		
CA 1985-473917		19850208		
ZA 1985-1093		19850213		
EP 1985-301125		19850220		
JP 1985-31662		19850221		
US 1986-894314		19860807		
CA 1987-473917		19870211		
OS MARPAT 113:131891				
GI				

L14 ANSWER 97 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

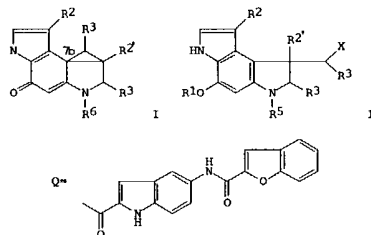
PAGE 1-A



PAGE 1-B



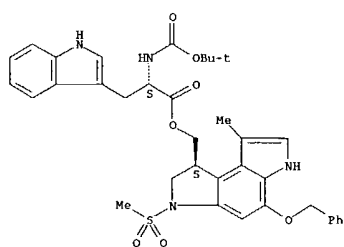
L14 ANSWER 98 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



AB Title compds. I and II [R1 = Me, CH2Ph, allyl, CH25Me, CH2OMe, CH2CH2CH2OMe, CH2CCl3, CH2CH2Si(R2)3, H; R2, R2', R3 = H, alkyl, Ph;  
 X = Cl, Br, iodo, OSO2R4; R4 = alkyl, Ph, tolyl, C6H4Br, C6H4NO2, CF3; R5 = various carbonyl acyl groups, many containing 1-2 indole and 1-2 amide subunits; R6 = H, R5] were prepared. For example, one optical isomer of II (R1 = CH2Ph, R2 = Me, R2' = R3 = H, X = OH, R5 = SO2Me) underwent demesylation, amidation with 5-(2-benzofuranyl carbonylamino)indole-2-carboxylic acid, O-mesylation, conversion to the chloromethyl compound, debenzoylation, and cyclization of the chloride to give (7bR, 8aS)-I (R2 = Me, R2' = R3 = H, R6 = acyl group Q) (III). A single i.v. dose of III in mice gave a 61% increase in lifespan after s.c. implantation of B16 melanoma. Fifty synthetic examples and addnl. antitumor results are given.  
 IT 101151-48-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and hydrolysis of)  
 RN 101151-48-8 CAPLUS  
 CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [1,2,3,6-tetrahydro-8-methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl)methyl ester, (S)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry.

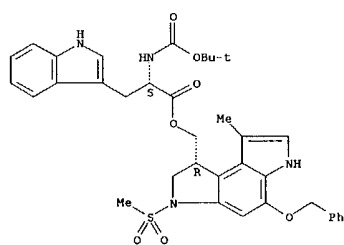
10/069,202

L14 ANSWER 98 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

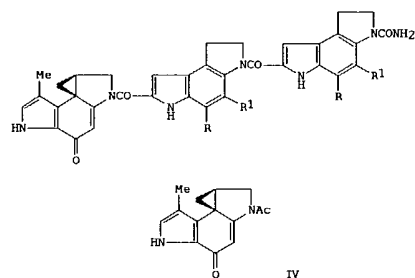


IT 101151-49-9P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)  
 RN 101151-49-9 CAPLUS  
 CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-,  
 [1,2,3,6-tetrahydro-8-  
 methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-  
 yl)methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 99 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1990:458759 CAPLUS  
 DN 113:58759  
 TI Sequence specificity of DNA alkylation by the unnatural enantiomer of  
 CC-1065 and its synthetic analogs  
 AU Hurley, Laurence H.; Warpehowski, Martha A.; Lee, Chong Soon;  
 McGovern, J.  
 Patrick; Scahill, Terrence A.; Kelly, Robert C.; Mitchell, Mark A.;  
 Wicnienski, Nancy A.; Gebhard; Ilse; et al.  
 CS Coll. Pharm., Univ. Texas, Austin, TX, 78712, USA  
 SO Journal of the American Chemical Society (1990), 112(12), 4633-49  
 CODEN: JACSAT; ISSN: 0002-7863  
 DT Journal  
 LA English  
 OS CASREACT 113:58759  
 GI



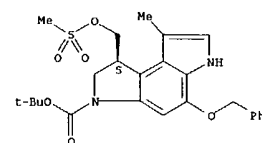
AB (-)-CC-1065, (I, R = OMe, R1 = OH; II), the unnatural enantiomer of  
 the potent and sequencespecific, DNA-reactive antibiotic, (+)-CC-1065  
 (III), was prepared and its covalent reaction with DNA was studied and  
 compared to that of III. Although II also formed covalent adducts in which the  
 cyclopropyl C was bonded to the N-3 atom of adenine, and the thermal  
 strand breakage that it produced paralleled that seen for III, it  
 lay in the opposite direction along the minor groove and exhibited a  
 markedly different sequence requirement for the covalently modified adenine.  
 While

L14 ANSWER 98 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L14 ANSWER 99 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 II and its analog, (-)-AB'C' (I, R = R1 = H), reacted readily at  
 adenines near to, but generally distinct from, adenines affected by III, and  
 exhibited potent cytotoxicity, their simpler analogs did not alkylate  
 DNA under the conditions employed and were biol. nonpotent. At relatively  
 high concns., the smallest such analog, (-)-A, (IV) reacted detectably  
 only at the same sites selected by III. An anal. of the reactivity  
 patterns of II and III and their analogs with DNA restriction  
 fragments supported the conclusion that the mode of sequence recognition for II  
 adduct formation is fundamentally different from that of III and is  
 primarily controlled by specific minor groove, AT-selective binding  
 interactions, rather than by sequence requirements of the covalent  
 step, as occurs for III and the (+)-CPI analogs. Models are proposed  
 comparing the interactions of the enantiomeric alkylating moieties variously  
 oriented in the minor groove at potential reaction sites. The  
 evolutionary significance of both the alkylating moiety and the minor  
 groove binding segments of the natural product is discussed.

IT 110314-49-3P 112836-68-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (preparation and chlorination of)  
 RN 110314-49-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-  
 1,6-dihydro-8-methyl-1-  
 [(methylsulfonyl)oxy)methyl]-5-(phenylmethoxy)-, 1,1-dimethylethyl  
 ester,  
 (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

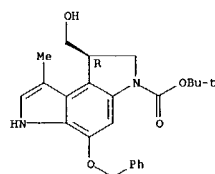


RN 112836-68-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-  
 (hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester,  
 (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

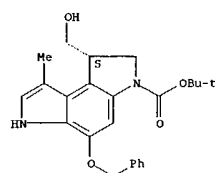
10/069,202

L14 ANSWER 99 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



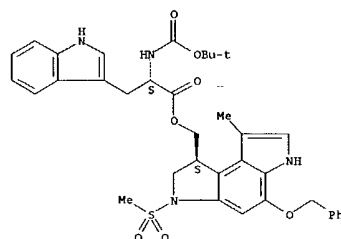
IT 112036-67-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (preparation and mesylation of)  
 RN 112036-67-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



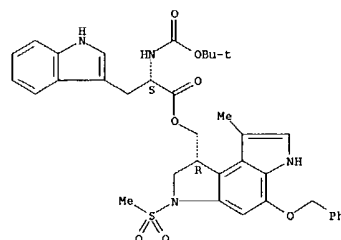
IT 110314-50-6P 112764-69-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (preparation and reduction of)  
 RN 110314-50-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)- (9CI)

L14 ANSWER 99 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 101151-49-9 CAPLUS  
 CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [1,2,3,6-tetrahydro-8-methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl)methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

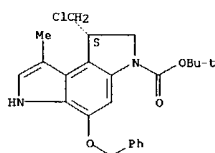


RN 108859-63-8 CAPLUS  
 CN D-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [1,2,3,6-tetrahydro-8-methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl)methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

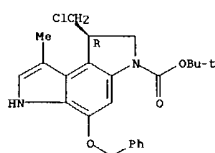
L14 ANSWER 99 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 (CA INDEX NAME)

Absolute stereochemistry.



RN 112764-69-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (R)- (9CI) (CA INDEX NAME)

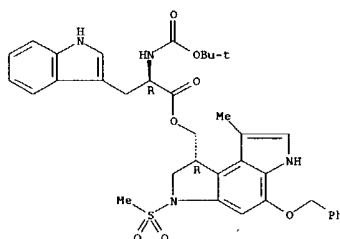
Absolute stereochemistry.



IT 101151-48-8P 101151-49-9P 108859-63-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (preparation and saponification of)  
 RN 101151-48-8 CAPLUS  
 CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [1,2,3,6-tetrahydro-8-methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl)methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 99 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 101151-49-9 CAPLUS  
 CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [1,2,3,6-tetrahydro-8-methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl)methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

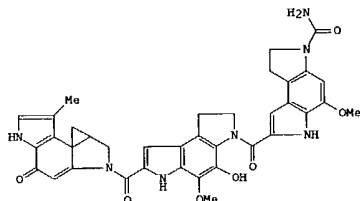


RN 108859-63-8 CAPLUS  
 CN D-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [1,2,3,6-tetrahydro-8-methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl)methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/069,202

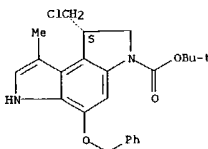
L14 ANSWER 100 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1990:400153 CAPLUS  
 DN 113:153  
 TI Synthesis and evaluation of aborted and extended CC-1065 functional analogs: (+)- and (-)-CPI-PDE-11, (+)- and (-)-CPI-CDP11, and (+)-, (+)-, and (-)-CPI-CDP13. Preparation of key partial structures and definition of an additional functional role of the CC-1065 central and right-hand subunits  
 AU Boger, Dale L.; Coleman, Robert S.; Invergo, Benedict J.; Sakya, Subas M.; Ishizaki, Takayoshi; Munk, Stephen A.; Zarrinmayeh, Hamideh; Kitos, Paul  
 CS Dep. Chem., Purdue Univ., West Lafayette, IN, 47907, USA  
 SO Journal of the American Chemical Society (1990), 112(12), 4623-32  
 CODEN: JACSAT; ISSN: 0002-7863  
 DT Journal  
 LA English  
 OS CASREACT 113:153  
 GI



AB Aborted and extended analogs of the antitumor antibiotic CC-1065 (NSC 298223) (I) were prepared and tested for in vitro cytotoxicity (L1210 cells) and DNA binding. Covalent alkylation of DNA by the analogs and the structural features required for such action are discussed.  
 IT 110314-50-6 112764-69-9  
 RL: RCT (Reactant); RACT (Reactant or reagent) (catalytic hydrogenolysis of, benzyl ether removal by)  
 RN 110314-50-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)- (9CI)

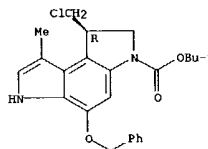
L14 ANSWER 100 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 (CA INDEX NAME)

Absolute stereochemistry.



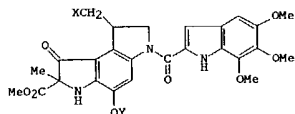
RN 112764-69-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (R)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



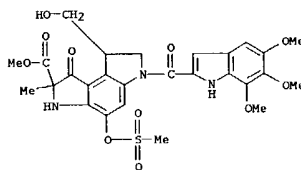
L14 ANSWER 101 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1990:197974 CAPLUS  
 DN 112:197974  
 TI Preparation of antitumor antibiotic SF2582C derivatives  
 IN Koyama, Masao; Ohba, Kazunori; Nakazawa, Tadashi; Yamamoto, Haruo; Sezaki, Masaji; Kondo, Shinichi  
 PA Meiji Seika Kaisha, Ltd., Japan  
 SO Eur. Pat. Appl., 7 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 339681	A2	19891102	EP 1989-107799	19890428
EP 339681	A3	19900131		
EP 339681	B1	19930331		
R: DE, FR, GB				
JP 01275581	A2	19891106	JP 1988-103782	19880428
JP 2562935	B2	19961211		
PRAI JP 1988-103782		19880428		
OS MARPAT 112:197974				
GI				



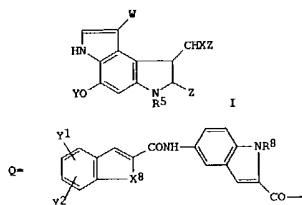
AB Antibiotic SF2582C derivs. (I; X, Y = RSO<sub>2</sub>; R = tolyl, Me, OH, H; excluding X = Y = X) are prepared, having an intense antitumor activity, while the parent antibiotic SF2582C lacks the antitumor activity. Thus, 40 mg antibiotic SF2582C (II) (isolated from a Streptomyces SF2582 strain) was treated with (MeSO<sub>2</sub>)<sub>2</sub>O in DMF containing Et<sub>3</sub>N to give, after silica gel chromatog., 41 mg I (X = Y = MeSO<sub>2</sub>) (III) and 6.3 mg II monomethanesulfonate (IV). III and IV increased the life span of mice transplanted with P-388 tumor cells by 54% at 21 mg/kg and 40% at 1 mg/kg, resp.  
 IT 126590-90-7P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

L14 ANSWER 101 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 (prepn. of, as antitumor agent)  
 RN 126590-90-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-4-[(methylsulfonyl)oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

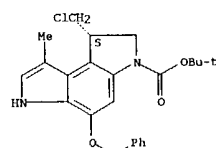


L14 ANSWER 102 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1989:154043 CAPLUS  
 DN 110:154043  
 TI Preparation of novel Antibiotic CC 1065 analogs as antitumor agents  
 IN Kelly, Robert C.; Martin, David G.; Aristoff, Paul A.  
 FA Upjohn Co., USA  
 SO PCT Int. Appl., 68 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8804659	A2	19880630	WO 1987-US3227	19871211
WO 8804659	A3	19880714		
W: AU, DK, FI, JP, KR, NO, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8812290	A1	19880715	AU 1988-12290	19871211
AU 617304	B2	19911128		
EP 340243	A1	19891108	EP 1988-90185	19871211
EP 340243	B1	19940928		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 02502005	T2	19900705	JP 1988-501400	19871211
US 5332837	A	19940726	US 1993-10526	19930122
FRAI US 1986-944633 19861219				
WO 1987-US3227 19871211				
US 1989-382159 19890608				
US 1990-554931 19900718				
US 1991-674422 19910322				
US 1992-845762 19920302				
OS MARPAT 110:154043				
GI				

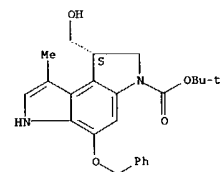


L14 ANSWER 102 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 112836-67-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

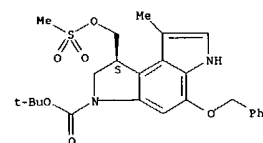
Absolute stereochemistry.



L14 ANSWER 102 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

AB The title compds. [I; R5 = 22 general acyl and 68 combinations thereof e.g. Q; W, Z = H, alkyl, Ph; X = N3, halo, cyanato, isocyanato, etc.; X8 = O, S, NH; Y = H, COR, CSR, CO2R1, SO2R1, CONR2R3, CSNR2R3, CONHSO2R4; Y1, Y2 = H, halo, alkyl, alkoxy, etc.; R = alkyl, alkenyl, alkynyl, (un)substituted Ph, naphthyl; R1 = alkyl, (un)substituted Ph; R2, R3 = H, alkyl, (un)substituted Ph; R4 = alkyl, (un)substituted Ph, naphthyl; R8 = H, Me, Et] were prepared I (R5 = Q; R8 = Y = Y1 = Y2 = Z = H; W = Me; X = Cl) was stirred 30 min at 5° with AcCl in pyridine to give I (as above except that Y = Ac) which caused a 30-day survival in 4 out of 6 mice inoculated with P388 leukemia i.p. at 0.20 mg/kg i.v.  
 IT 110314-49-3P 110314-50-6P 112836-67-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and reaction of, in preparation of antitumor agents)  
 RN 110314-49-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-8-methyl-5-[(methylsulfonyl)oxy]methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

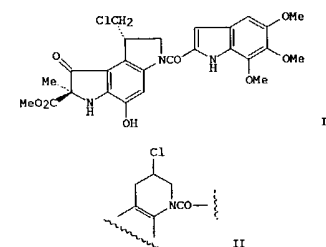


RN 110314-50-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

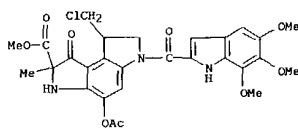
L14 ANSWER 103 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1989:72198 CAPLUS  
 DN 110:72198  
 TI Pyrindamycins A and B, new antitumor antibiotics  
 IN Ohba, Kazunori; Watabe, Hiroomi; Sasaki, Toru; Takeuchi, Yasuo; Kodama, Yoshio; Nakazawa, Tadashi; Yamamoto, Haruo; Shomura, Takashi; Sezaki, Masaji; Kondo, Shinichi  
 CS Res. Lab., Meiji Seika Kaisha, Ltd., Yokohama, 222, Japan  
 SO Journal of Antibiotics (1989), 41(10), 1515-19  
 CODEN: JANTAJ; ISSN: 0021-8820  
 DT Journal  
 LA English  
 GI



AB Pyrindamycins A (I) and B (II) were isolated from the culture broth of Streptomyces sp. SF2582, their structures were determined and they exhibited activity against both gram-pos. and -neg. bacteria. Marked increases in life span were observed with single i.p. treatment of I and II against mice i.p. implanted with P388 leukemia.  
 IT 110462-85-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)  
 RN 110462-85-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 4-(acetyloxy)-8-(chloromethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

L14 ANSWER 103 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 104 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1988:437665 CAPLUS

DN 109:37665

TI Total synthesis of (i)-N2-(phenylsulfonyl)-CPI, (i)-CC-1065, (+)-CC-1065, ent-(+)-CC-1065, and the precise, functional agents (i)-CPI-CDPI2, (+)-CPI-CDPI2, and (-)-CPI-CDPI2 [(i)-(3bR\*,4aS\*)-, (+)-(3bR,4aS\*)-, and (-)-(3bS,4aR)-deoxy-CC-1065]

AU Eoger, Dale L.; Coleman, Robert S.

CS Dep. Chem., Purdue Univ., West Lafayette, IN, 47907, USA

SO Journal of the American Chemical Society (1988), 110(14), 4796-807

CODEN: JACSAT; ISSN: 0002-7863

DT Journal

LA English

OS CASREACT 109:37665

AB The title compds. were prepared. Left-hand segment is based on the regioselective, nucleophilic addition of 1-piperidino-1-propene to the selectively activated N4-(phenylsulfonyl)-p-quinone diimide for direct introduction of the 3-methylpyrrole A ring and the subsequent implementation of a 5-exo-dig aryl radical-alkyne cyclization for indirect

introduction of the 3-(hydroxymethyl)pyrrole C ring.

Spirocyclization

gave the spirocyclopropylquinone. CPI-CDPI2 has the structural and functional features that are responsible for the sequence-selective

B-DNA

minor groove association and the potent cytostatic activity of

CC-1065. Both

CC-1065 and CPI-CDPI2 constitute reactive alkylating agents

superimposed

on the CDPI trimer skeleton and derive their B-DNA associating

properties

through hydrophobic binding-driven bonding. It is predominantly

hydrophobic interactions of the concave face of CC-1065 and its B-DNA

minor-groove complementary shape that permit the association with

AT-rich

minor-groove regions and promote the irreversible adenine N-3 covalent

alkylation.

IT 112836-67-6P 112836-68-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(preparation and chlorination of)

RN 112836-67-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-

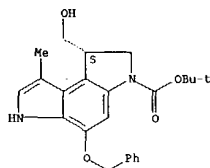
(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester,

(S)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 104 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 112836-68-7 CAPLUS

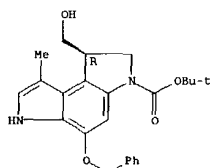
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-

(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl

ester, (R)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 110314-50-6P 112764-69-9P 175614-07-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(preparation and debenzoylation of)

RN 110314-50-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,

1-(chloromethyl)-1,6-

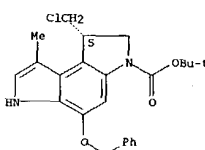
dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-

(9CI)

(CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 104 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 112764-69-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,

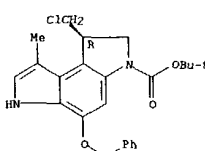
1-(chloromethyl)-1,6-

dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (R)-

(9CI)

(CA INDEX NAME)

Absolute stereochemistry.



RN 175614-07-0 CAPLUS

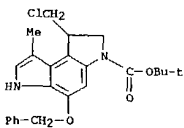
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,

1-(chloromethyl)-1,6-

dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI)

(CA

INDEX NAME)



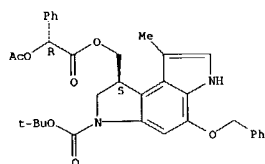
IT 112764-68-8P 112793-57-4P

10/069,202

L14 ANSWER 104 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

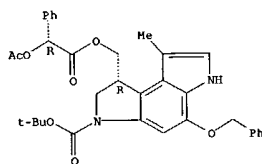
RACT (Reactant or reagent)  
(prepn. and ester hydrolysis of)  
RN 112764-69-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-  
[[[(acetyloxy)phenylacetyl]oxy]methyl]-1,6-dihydro-8-methyl-5-  
(phenylmethoxy)-, 1,1-dimethylethyl ester, [R-(R\*,S\*)]- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



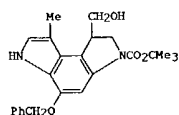
RN 112793-57-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-  
[[[(acetyloxy)phenylacetyl]oxy]methyl]-1,6-dihydro-8-methyl-5-  
(phenylmethoxy)-, 1,1-dimethylethyl ester, [R-(R\*,R\*)]- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



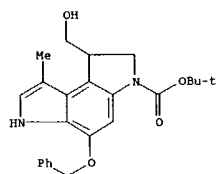
IT 112089-71-1P  
RL: SPN (Synthetic preparation); PREP (Preparation)

L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1988:437661 CAPLUS  
DN 109:37661  
TI Total synthesis of (+)- and (-)-CPI-CDPI2: (+)-(3bR,4aS)- and  
(-)-(3bS,4aR)-deoxy-CC-1065  
AU Boyer, Dale L.; Coleman, Robert S.  
CS Dep. Chem., Purdue Univ., West Lafayette, IN, 47907, USA  
SO Journal of Organic Chemistry (1988), 53(3), 695-8  
CODEN: JOCEAH; ISSN: 0022-3263  
DT Journal  
LA English  
OS CASREACT 109:37661  
GI



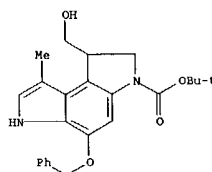
AB The title compds. [(+)- and (-)-I] were obtained in high enantiomeric  
purity by a sequence involving resolution of the intermediate II via  
an optically active ester. (+)-I and (-)-I have antitumor ED50 of 3.9  
+ 10-6 and 1.2 + 10-5 µg/mL, resp., against P388 leukemia.

IT 112089-71-1  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(esterification with, of optically active carboxylic acids)  
RN 112089-71-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-  
(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester  
(9CI) (CA INDEX NAME)



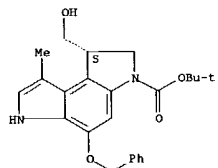
IT 112836-67-6P 112836-68-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT

L14 ANSWER 104 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
(prepn. and resolu. of)  
RN 112089-71-1 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-  
(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester  
(9CI) (CA INDEX NAME)



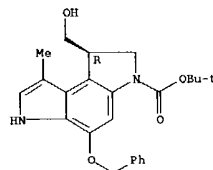
L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
(Reactant or reagent)  
(prepn. and chlorination of)  
RN 112836-67-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-  
(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester,  
(S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 112836-68-7 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-  
(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester,  
(R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



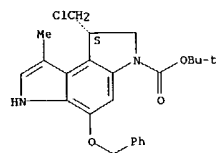
IT 110314-50-6P 112764-69-9P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT (Reactant or reagent)  
(preparation and deblocking of)  
RN 110314-50-6 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
1-(chloromethyl)-1,6-  
dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-  
(9CI)



10/069,202

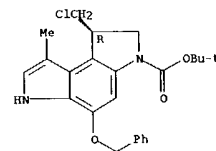
L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
(CA INDEX NAME)

Absolute stereochemistry.



RN 112764-69-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (R)- (9CI) (CA INDEX NAME)

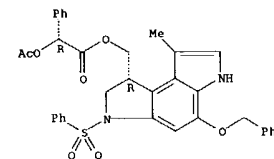
Absolute stereochemistry.



IT 112764-68-8P 112793-57-4P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACIT (Reactant or reagent)  
(preparation and ester hydrolysis of)  
RN 112764-68-8 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[[[(acetyloxy)phenylacetyl]oxy]methyl]-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, [R-(R\*,S\*)]- (9CI) (CA INDEX NAME)

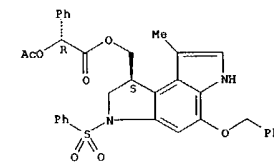
Absolute stereochemistry.

L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



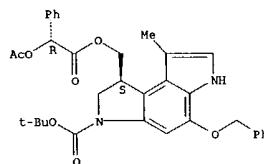
RN 114928-10-8 CAPLUS  
CN Benzeneacetic acid, α-(acetyloxy)-, [1,2,3,6-tetrahydro-8-methyl-5-(phenylmethoxy)-3-(phenylsulfonyl)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, [R-(R\*,S\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



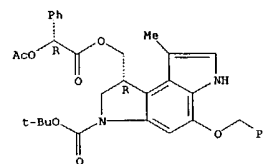
RN 114928-11-9 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-8-methyl-1-[[[[[5-methyl-2-(1-methylethyl)cyclohexyl]oxy]acetyl]oxy]methyl]-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, [1R-[1α(R\*),2β,5α]]- (9CI) (CA INDEX NAME)

L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 112793-57-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[[[(acetyloxy)phenylacetyl]oxy]methyl]-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, [R-(R\*,R\*)]- (9CI) (CA INDEX NAME)

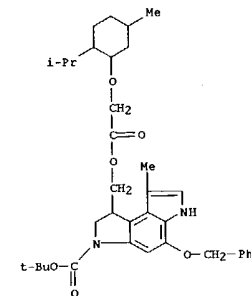
Absolute stereochemistry.



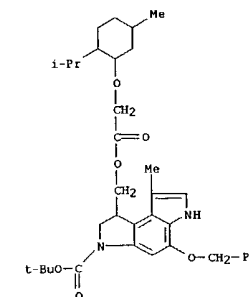
IT 114928-09-5P 114928-10-8P 114928-11-9P  
114928-12-0P 114928-13-1P 114928-14-2P  
114928-15-3P 114928-16-4P 114928-17-5P  
114928-18-6P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)  
RN 114928-09-5 CAPLUS  
CN Benzeneacetic acid, α-(acetyloxy)-, [1,2,3,6-tetrahydro-8-methyl-5-(phenylmethoxy)-3-(phenylsulfonyl)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, [R-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 114928-12-0 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-8-methyl-1-[[[[[5-methyl-2-(1-methylethyl)cyclohexyl]oxy]acetyl]oxy]methyl]-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, [1R-[1α(S\*),2β,5α]]- (9CI) (CA INDEX NAME)



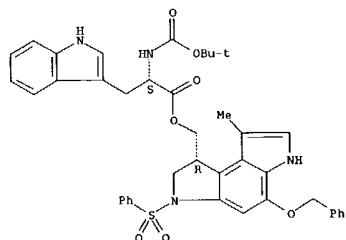
RN 114928-13-1 CAPLUS

10/069,202

L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-,  
[1,2,3,6-tetrahydro-8-

methyl-5-(phenylmethoxy)-3-(phenylsulfonyl)benzo[1,2-b:4,3-b']dipyrrol-1-yl)methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

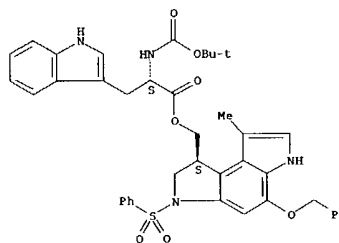


RN 114928-14-2 CAPLUS  
CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-,  
[1,2,3,6-tetrahydro-8-

methyl-5-(phenylmethoxy)-3-(phenylsulfonyl)benzo[1,2-b:4,3-b']dipyrrol-1-yl)methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

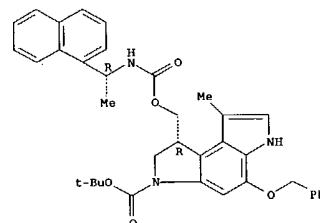
L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 114928-15-3 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
1,6-dihydro-8-methyl-1-

[[[[(1-(1-naphthalenyl)ethyl)amino]carbonyl]oxy]methyl]-5-(phenylmethoxy)-,  
1,1-dimethylethyl ester, [R-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

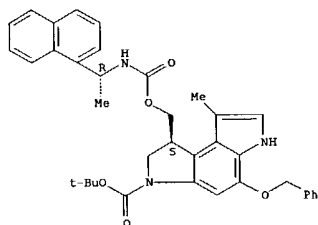


RN 114928-16-4 CAPLUS  
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
1,6-dihydro-8-methyl-1-

[[[[(1-(1-naphthalenyl)ethyl)amino]carbonyl]oxy]methyl]-5-(phenylmethoxy)-

L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
1,1-dimethylethyl ester, [R-(R\*,S\*)]- (9CI) (CA INDEX NAME)

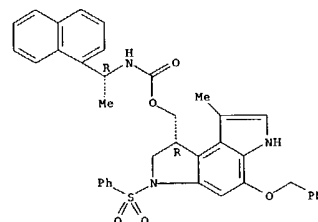
Absolute stereochemistry.



RN 114928-17-5 CAPLUS  
CN Carbamic acid, [1-(1-naphthalenyl)ethyl]-,  
[1,2,3,6-tetrahydro-8-methyl-5-

(phenylmethoxy)-3-(phenylsulfonyl)benzo[1,2-b:4,3-b']dipyrrol-1-yl)methyl  
ester, [R-(R\*,R\*)]- (9CI) (CA INDEX NAME)

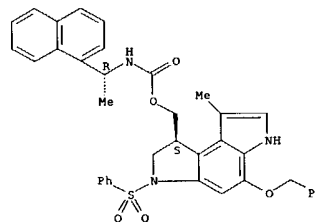
Absolute stereochemistry.



RN 114928-18-6 CAPLUS  
CN Carbamic acid, [1-(1-naphthalenyl)ethyl]-,  
[1,2,3,6-tetrahydro-8-methyl-5-

(phenylmethoxy)-3-(phenylsulfonyl)benzo[1,2-b:4,3-b']dipyrrol-1-yl)methyl  
ester, [R-(R\*,S\*)]- (9CI) (CA INDEX NAME)

L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
Absolute stereochemistry.



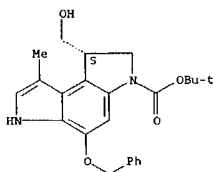
L14 ANSWER 106 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1988:112038 CAPLUS  
 DN 108:112038  
 TI Total synthesis of (+)-CC-1065 and ent-(-)-CC-1065  
 AU Roger, Dale L.; Coleman, Robert S.  
 CS Dep. Chem., Purdue Univ., West Lafayette, IN, 47907, USA  
 SO Journal of the American Chemical Society (1988), 110(4), 1321-3  
 CODEN: JACSAT; ISSN: 0002-7863  
 DT Journal  
 LA English  
 OS CASREACT 108:112038  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The spirobicyclo[5.2.0]octa-2,5-dien-4-one left-hand segment I of CC-1065 was prepared and its immediate precursor II resolved and coupled with synthetic PDE-I dimer in the total syntheses of natural (+)-CC-1065 (III) and unnatural ent-(-)-CC-1065. The approach to I is based on the regioselective, nucleophilic addition of 1-piperidino-1-propene to a selectively activated N4-benzenesulfonyl p-quinonediimide for direct, 3-methylpyrrole introduction, implementation of a 5-exo-dig aryl radical-alkyne cyclization for indirect 3-hydroxymethylindoline introduction and resolution of II. The Winstein Ar-3' cyclization was used for final introduction of the reactive, electrophilic spirocyclopropane. III and its isomer have the same antitumor activity.  
 IT 112836-67-6P 112836-68-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and chlorination of)  
 RN 112836-67-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-(9CI) (CA INDEX NAME)

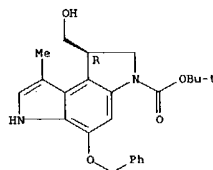
Absolute stereochemistry.

L14 ANSWER 106 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 112836-68-7 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (R)-(9CI) (CA INDEX NAME)

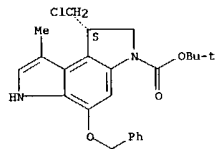
Absolute stereochemistry.



IT 110314-50-6P 112764-69-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and deblocking of)  
 RN 110314-50-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-(9CI) (CA INDEX NAME)

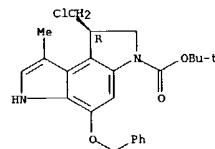
Absolute stereochemistry.

L14 ANSWER 106 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 112764-69-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (R)-(9CI) (CA INDEX NAME)

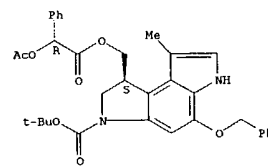
Absolute stereochemistry.



IT 112764-68-8P 112793-57-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and ester hydrolysis of)  
 RN 112764-68-8 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[[[(acetyloxy)phenylacetyl]oxymethyl]-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, [R-(R\*,S\*)]-(9CI) (CA INDEX NAME)

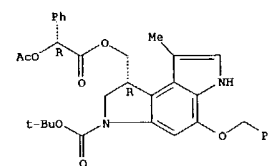
Absolute stereochemistry.

L14 ANSWER 106 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 112793-57-4 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[[[(acetyloxy)phenylacetyl]oxymethyl]-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, [R-(R\*,R\*)]-(9CI) (CA INDEX NAME)

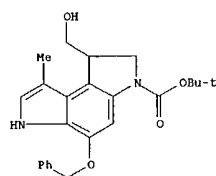
Absolute stereochemistry.



IT 112089-71-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and esterification of)  
 RN 112089-71-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

10/069,202

L14 ANSWER 106 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

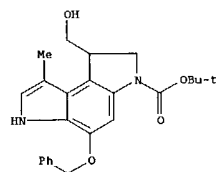


L14 ANSWER 107 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1988:94431 CAPLUS  
 DN 108:94431  
 TI Stereoelectronic factors influencing the biological activity and DNA interaction of synthetic antitumor agents modeled on CC-1065  
 AU Warpehoski, M. A.; Gebhard, I.; Kelly, R. C.; Krueger, W. C.; Li, L. H.; McGovren, J. P.; Prairie, M. D.; Wicnienski, N.; Wierenga, W.  
 CS Res. Lab., Upjohn Co., Kalamazoo, MI, 49001, USA  
 SO Journal of Medicinal Chemistry (1988), 31(3), 590-603  
 CODEN: JMCHAR; ISSN: 0022-2623  
 UT Journal  
 LA English  
 OS CASREACT 108:94431  
 GI

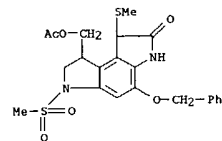
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The synthesis, physicochem. properties, and biol. activities of 21 novel spiro cyclopropyl compds., e.g. I [R = H, SO2Ph, CO2Me3, COMe, substituted (indol-2-yl)carbonyl], prepared by intramol. cyclopropanation of pyrroloindoles II (R1 = PhCH2, R2 = SO2CF3; R1 = R2 = H), are described.  
 Many I are more effective than the antitumor antibiotic CC-1065 (III) against murine tumors. In particular, IV exhibits high activity and potency. Structure-activity anal. supports a mol. mechanism of biol. action involving hydrophobic interaction of the drug with DNA and acid-catalyzed alkylation of DNA.  
 IT 112089-71-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and hydrogenolysis of)  
 RN 112089-71-1 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI)  
 (CA INDEX NAME)

L14 ANSWER 107 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

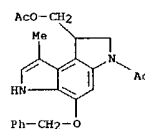


IT 112089-53-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and methylation of, stereochem. of)  
 RN 112089-53-9 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-2(1H)-one, 8-[(acetyloxy)methyl]-3,6,7,8-tetrahydro-6-(methylsulfonyl)-1-(methylthio)-4-(phenylmethoxy)- (9CI)  
 (CA INDEX NAME)



IT 112089-75-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and saponification of)  
 RN 112089-75-5 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 3-acetyl-1,2,3,6-tetrahydro-8-methyl-5-(phenylmethoxy)-, acetate (ester) (9CI) (CA INDEX NAME)

L14 ANSWER 107 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



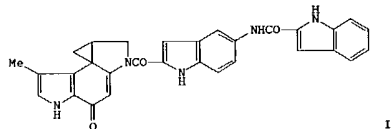
10/069,202

L14 ANSWER 108 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1987:597901 CAPLUS  
 DN 107:197901  
 TI Coupling of cyclopropylpyrrolindole (CPI) derivatives. The preparation of CC-1065, ent-CC-1065, and analogs  
 AU Kelly, Robert C.; Gebhard, Ilse; Wicnienski, Nancy; Aristoff, Paul A.; Johnson, Paul D.; Martin, David G.  
 CS Cancer and Viral Dis. Res., Upjohn Co., Kalamazoo, MI, 49001, USA  
 SO Journal of the American Chemical Society (1987), 109(22), 6837-8  
 CODEN: JACSAT; ISSN: 0002-7863  
 DT Journal  
 LA English  
 OS CASREACT 107:197901  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

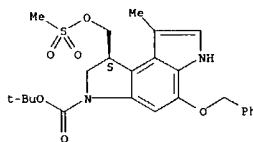
AB CC-1065 (I, R = R1) and its analogs I (R = pentyl, 2-indolyl, R2, X = NH, O) were prepared from the pyrrolindole II (R3 = OH, R4 = H, R5 = CH2Ph) via  
 II (R3 = Cl, R4 = CO2Me3, R5 = H), II (R3 = Cl, R4 = R5 = H), and II (R3 = Cl, R4 = COR, R5 = H). Ent-CC-1065 was similarly prepared and had an ED50  
 against leukemia L1210 of 4.5 + 10-12 g/mL.  
 IT 110314-49-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT  
 (Reactant or reagent)  
 (preparation and chlorination of)  
 RN 110314-49-3 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
 1,6-dihydro-8-methyl-1-  
 [(methylsulfonyl)oxy]methyl-5- (phenylmethoxy)-, 1,1-dimethylethyl  
 ester, (S)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry.

L14 ANSWER 109 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1987:423139 CAPLUS  
 DN 107:23139  
 TI Total synthesis of U-71184, a potent new antitumor agent modeled on CC-1065  
 AU Warpekhoski, M. A.  
 CS Upjohn Co., Kalamazoo, MI, 49001, USA  
 SO Tetrahedron Letters (1986), 27(35), 4103-6  
 CODEN: TELEAY; ISSN: 0040-4039  
 DT Journal  
 LA English  
 OS CASREACT 107:23139  
 GI

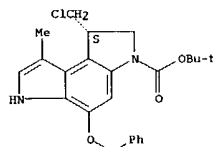


AB U-71184 (I), a highly potent analog of novel antitumor antibiotic CC-1065, involves the unmasking of a p-hydroxyphenethyl mesylate, which undergoes  
 facile intramol. elimination to afford the reactive cyclopropylpyrrolindole. Its enantiomer, U-71185, was also prepared. I had antitumor activity comparable to that of CC-1065 without the  
 delayed toxicity, but U-71185 was inactive.  
 IT 101151-48-8P 108859-63-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT  
 (Reactant or reagent)  
 (preparation and saponification of)  
 RN 101151-48-8 CAPLUS  
 CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [1,2,3,6-tetrahydro-8-  
 methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (S)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry.

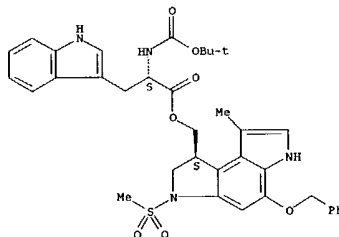
L14 ANSWER 108 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



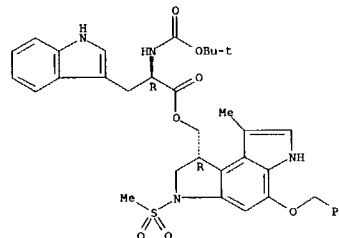
IT 110314-50-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT  
 (Reactant or reagent)  
 (preparation and hydrogenolysis of)  
 RN 110314-50-6 CAPLUS  
 CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,  
 1-(chloromethyl)-1,6-  
 dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-  
 (9CI) (CA INDEX NAME)  
 Absolute stereochemistry.



L14 ANSWER 109 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 108859-63-8 CAPLUS  
 CN D-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [1,2,3,6-tetrahydro-8-  
 methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (R)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry.

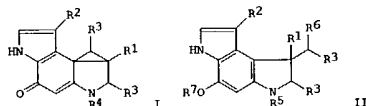


10/069,202

L14 ANSWER 110 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1986:148641 CAPLUS  
 DN 104:148641  
 TI Analogs of antibiotic CC-1065  
 IN Kelly, Robert Charles; Warpehoski, Martha Ann; Wierenga, Wendell  
 PA Upjohn Co., USA  
 SO Eur. Pat. Appl., 96 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CMT 2

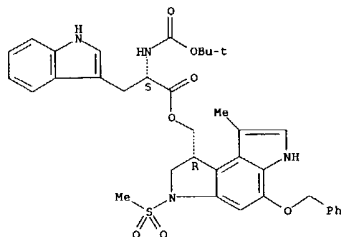
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 154445	A1	19850911	EP 1985-301125	19850220
EP 154445	B1	19890531		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
US 4912227	A	19900327	US 1986-894314	19860807
JP 08225573	A2	19960903	JP 1995-331640	19951220
PRAI US 1984-581836		19840221		
US 1985-694363		19850124		
CA 1985-473917		19850208		
ZA 1985-1093		19850213		
EP 1985-301125		19850220		
JP 1985-31662		19850221		

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AB Title compds. I and II (R1, R2, R3 = H, alkyl, phenyl; R4 = H, acyl; R5 = acyl; R6 = halo, substituted sulfonyloxy; R7 = Me, substituted Me) and their salts, useful as UV light absorbents, bactericides, and antitumors were prepared. Thus, II (R1 = R2 = R3 = H, R5 = mesyl, R7 = PhCH2) was N-demethylated, N-acetylated, O-mesylated, O-debenzylated, and cyclized to give I (R1 = R2 = R3 = H, R4 = Ac). The latter compound showed cytotoxic activity against murine L1210 tumor cells at 0.0048 µg/mL.  
 IT 101151-49-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

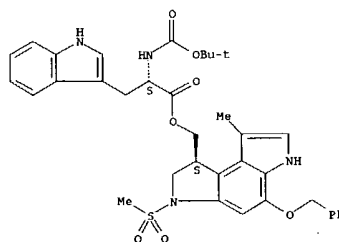
L14 ANSWER 110 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 110 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 (Reactant or reagent)  
 (prepn. and hydrolysis of)  
 RN 101151-48-8 CAPLUS  
 CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [1,2,3,6-tetrahydro-8-

methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl)methyl ester, (5)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 101151-49-9P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)  
 RN 101151-49-9 CAPLUS  
 CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [1,2,3,6-tetrahydro-8-

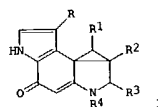
methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl)methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 111 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1984:156432 CAPLUS  
 DN 100:156432  
 TI 1,2,8,8A-Cyclopropa[c]benzo[1,2,-bi-4,3-b']dipyrrol-4(5H)-ones  
 IN Wierenga, Wendell  
 PA Upjohn Co., USA  
 SO U.S., 11 pp. Cont.-in-part of U.S. Ser. No. 207,839, abandoned.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CMT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4424365	A	19840103	US 1982-391055	19820622
DE 3142143	A1	19820624	DE 1981-3142143	19811023
DE 3142143	C2	19920730		
DE 3153725	C2	19930318	DE 1981-3153725	19811023
CH 655726	A	19860515	CH 1981-4003	19811028
CH 655724	A	19860515	CH 1981-6895	19811028
FR 2494273	A1	19820521	FR 1981-21480	19811117
FR 2494273	B1	19851220		
JP 57114589	A2	19820716	JP 1981-183170	19811117
JP 03010629	B4	19910214		
SU 1318165	A3	19870615	SU 1981-3353089	19811117
US 4400518	A	19830823	US 1982-346465	19820208
US 4413132	A	19831101	US 1982-346463	19820208
US 4423230	A	19831227	US 1982-346459	19820208
US 4423228	A	19831227	US 1982-346460	19820208
US 4423229	A	19831227	US 1982-346461	19820208
US 4431820	A	19840214	US 1982-346464	19820208
US 4496492	A	19850129	US 1983-515434	19830719
JP 03014581	A2	19910123	JP 1990-134241	19900525
JP 04065076	B4	19921016		
JP 03014545	A2	19910123	JP 1990-134242	19900525
JP 04060594	B4	19920928		
JP 03014561	A2	19910123	JP 1990-134243	19900525
JP 04027231	B4	19920511		
PRAI US 1980-207838		19801118		
CH 1981-6895		19811028		
US 1982-346642		19820208		
OS CASREACT 100:156432				

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AB The title compds. I (R-R3 = H, alkyl, Ph; R4 = SO2R5, CO2CH2R6; R5 = H,

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L14 ANSWER 111 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
alkyl, Ph, CH<sub>2</sub>OPh; R<sub>6</sub> = CH<sub>2</sub>, CC13, CH<sub>2</sub>SO<sub>2</sub>RS, Ph, fluorenylmethyl)

were  
prepd. Thus, I [R = Me, R<sub>1</sub>-R<sub>3</sub> = H, R<sub>4</sub> = SO<sub>2</sub>Me (II)] was prepd. from  
2,5-O<sub>2</sub>N(MeO)C<sub>6</sub>H<sub>3</sub>CH(CO<sub>2</sub>Et)<sub>2</sub> in 10 steps. II is a fragment of  
antibiotic  
CC-1065 and has an ED<sub>50</sub> against leukemia L1210 in vitro of 0.13  
µg/mL.

II also has bactericidal activity (no data).

IT 140862-50-6P 140862-51-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT  
(Reactant or reagent)  
(preparation and reduction of)

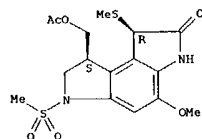
RN 140862-50-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrol-2(1H)-one, 8-[(acetyloxy)methyl]-3,6,7,8-  
tetrahydro-4-methoxy-6-(methylsulfonyl)-1-(methylthio)-, cis- (9CI)

(CA

INDEX NAME)

Relative stereochemistry.



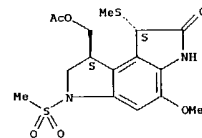
RN 140862-51-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrol-2(1H)-one, 8-[(acetyloxy)methyl]-3,6,7,8-  
tetrahydro-4-methoxy-6-(methylsulfonyl)-1-(methylthio)-, trans- (9CI)

(CA

INDEX NAME)

Relative stereochemistry.



L14 ANSWER 112 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1983:505087 CAPLUS

DN 99:105087

TI A versatile and efficient process to 3-substituted indoles from  
anilines

AU Wierenga, Wendell; Griffin, John; Warpehoski, Martha A.

CS Cancer Res., Upjohn Co., Kalamazoo, MI, 49001, USA

SO Tetrahedron Letters (1983), 24(24), 2437-40

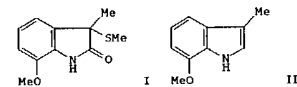
CODEN: TETLEA; ISSN: 0040-4039

DT Journal

LA English

OS CASREACT 99:105087

GI



AB Borane-mediated reductive elimination of α-methylthio-,  
α-hydroxy-, or α-alkoxy-α1-substituted oxindoles affords  
3-substituted indoles in high yield. Thus, treating oxindole I with  
Me<sub>2</sub>S-BH<sub>3</sub> or tetrahydrofuran-BH<sub>3</sub> gave 92% indole II.

IT 86915-20-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 86915-20-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol,

1,2,3,6-tetrahydro-5-methoxy-8-

methyl-3-(methylsulfonyl)-, acetate (ester) (9CI) (CA INDEX NAME)

